

Figure 1

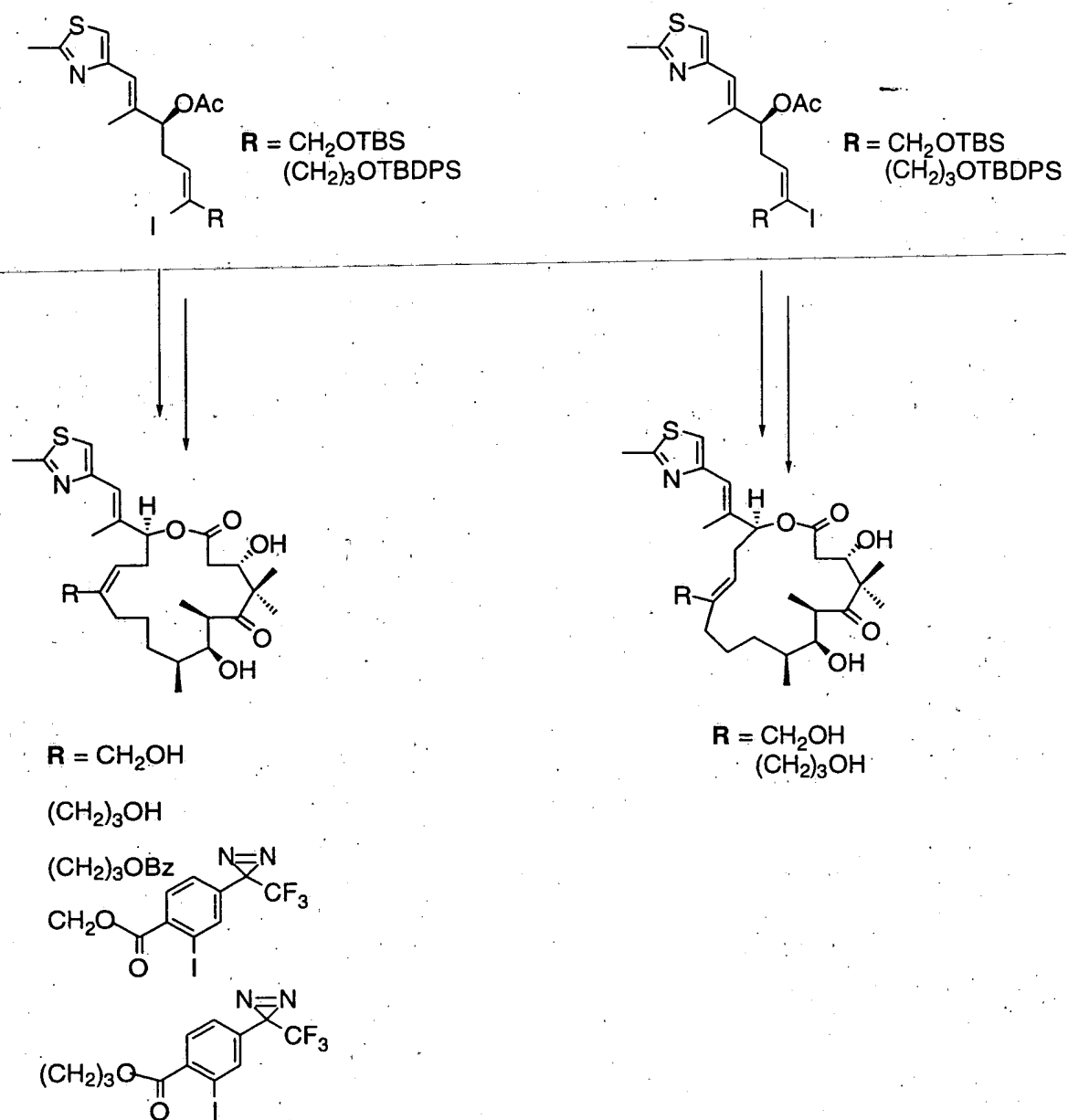


Figure 2

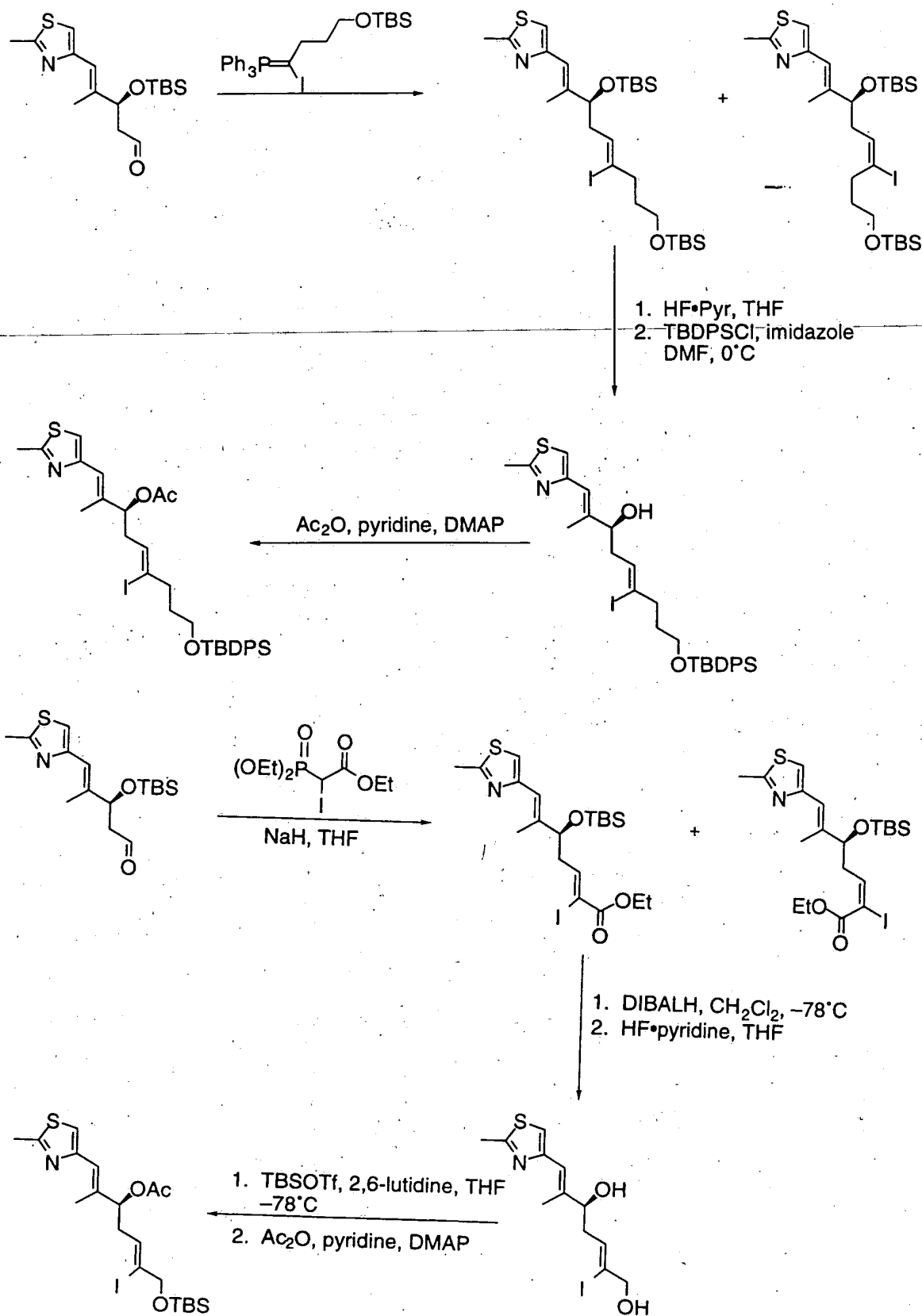


Figure 3(A)

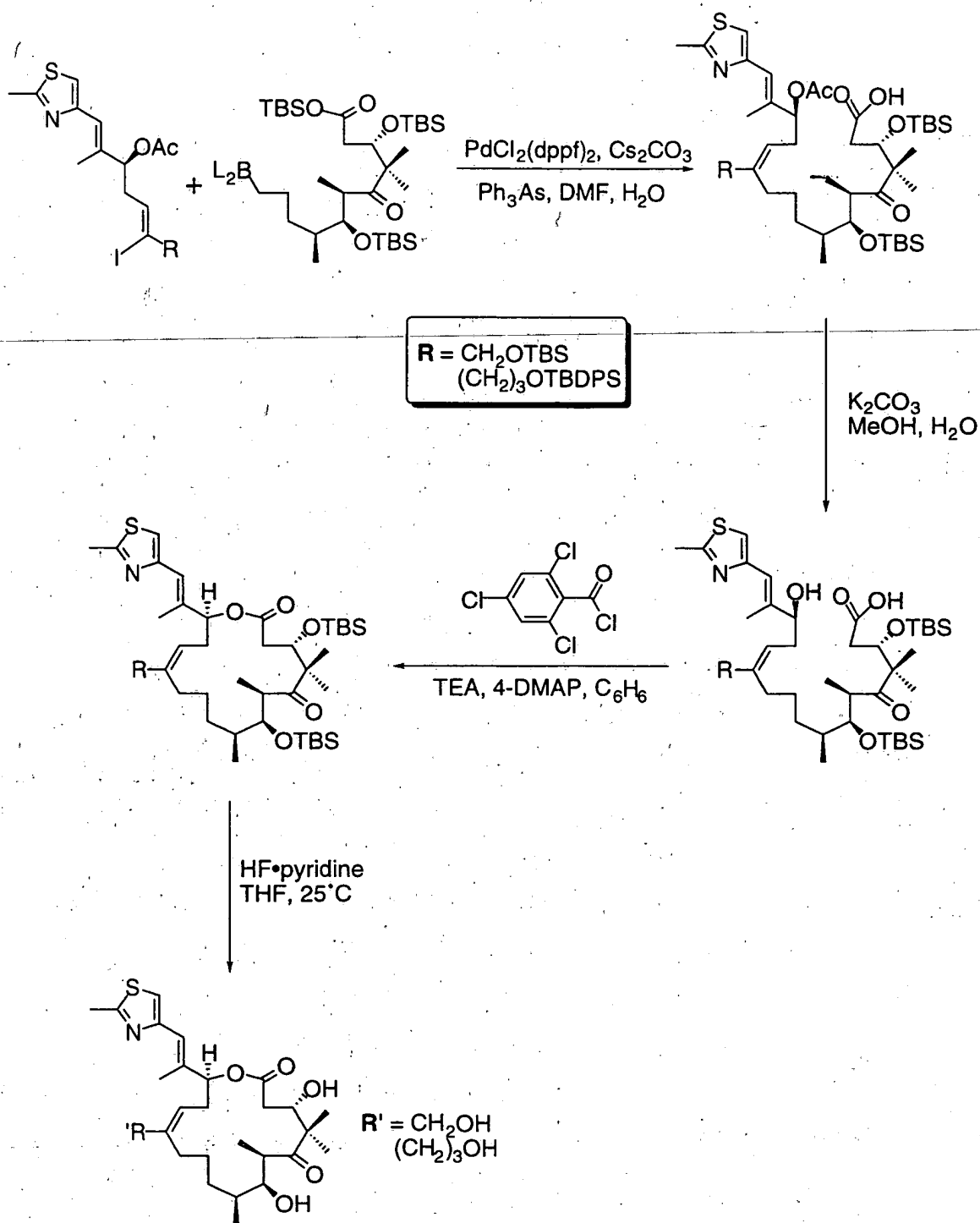


Fig. 3(B)

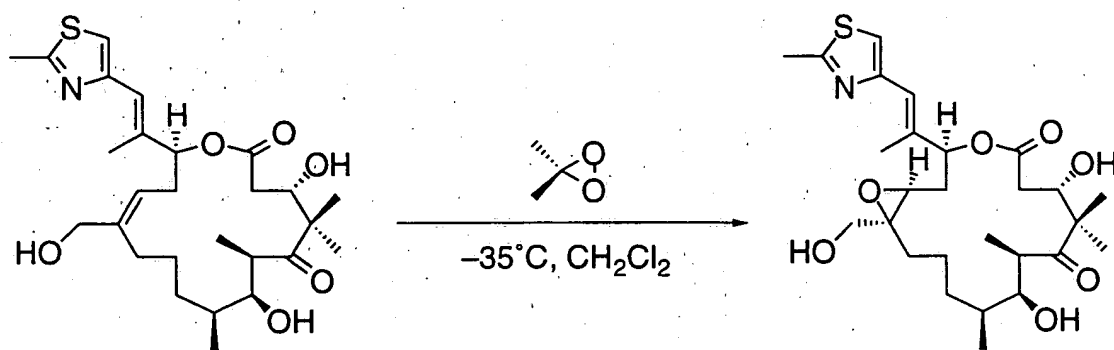
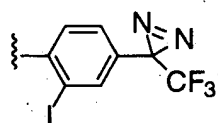
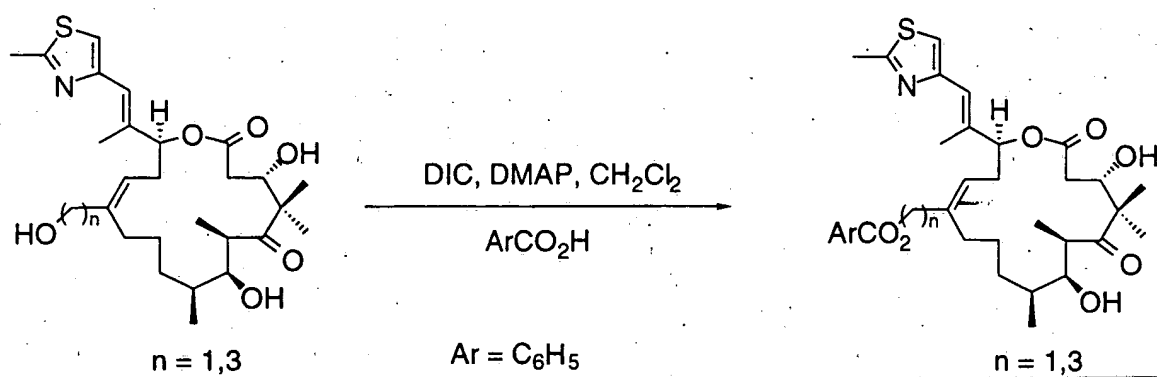


Fig. 3(C)

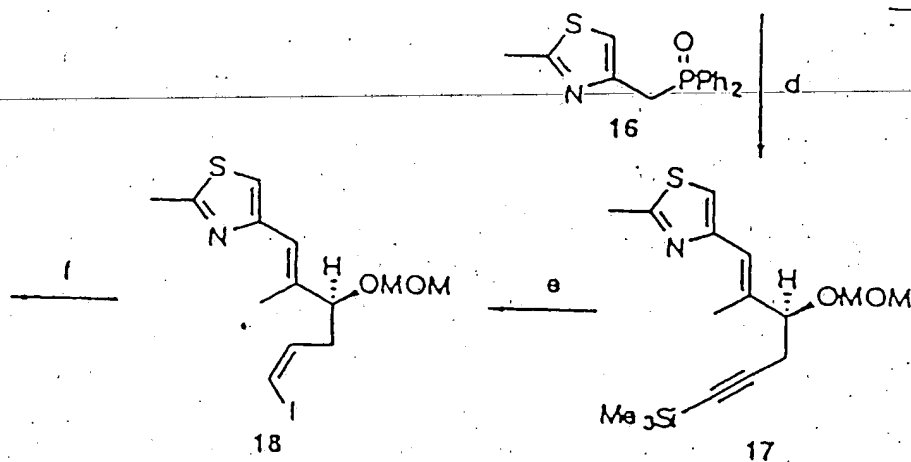
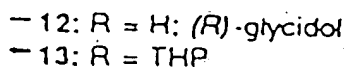


Figure 4

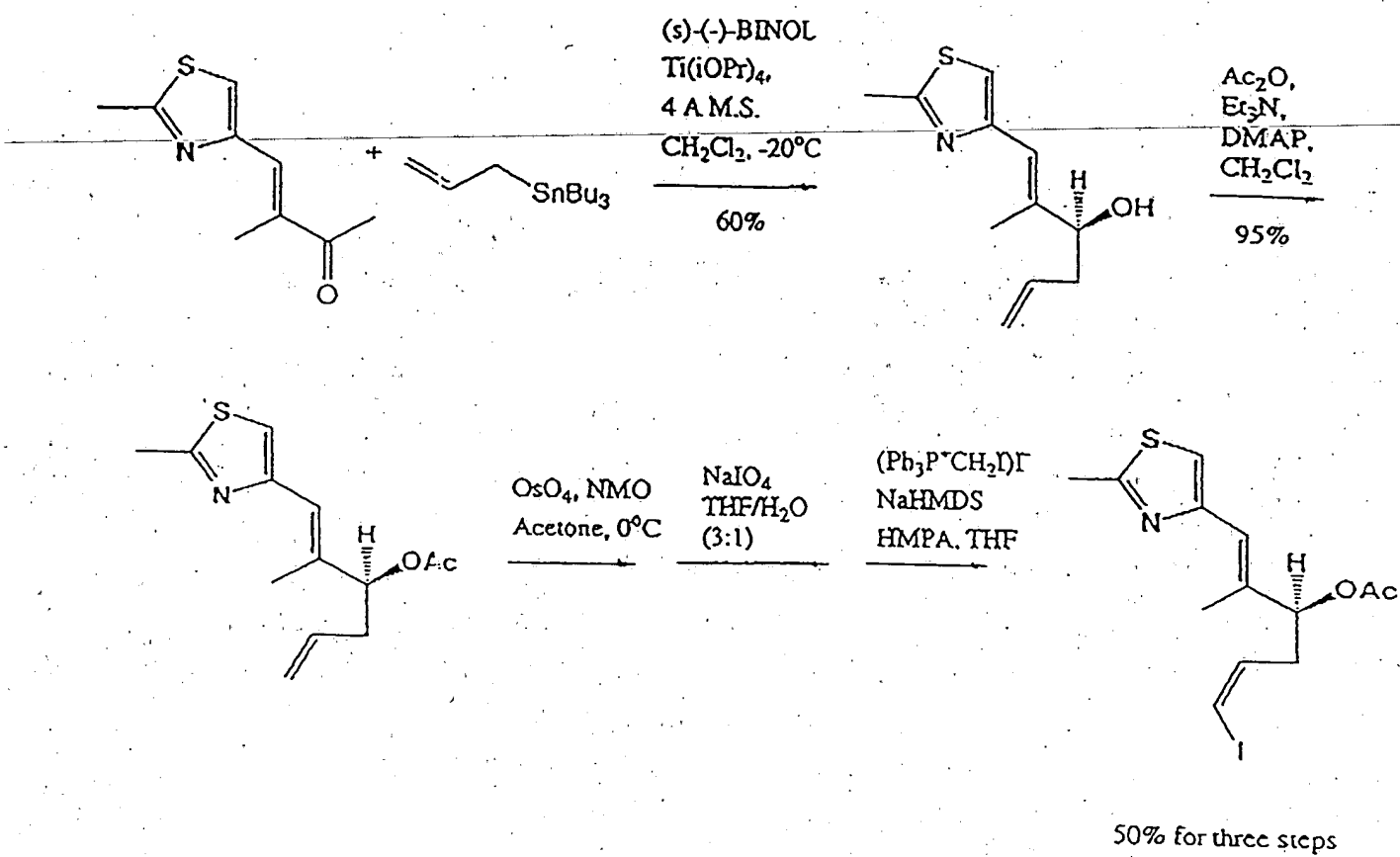
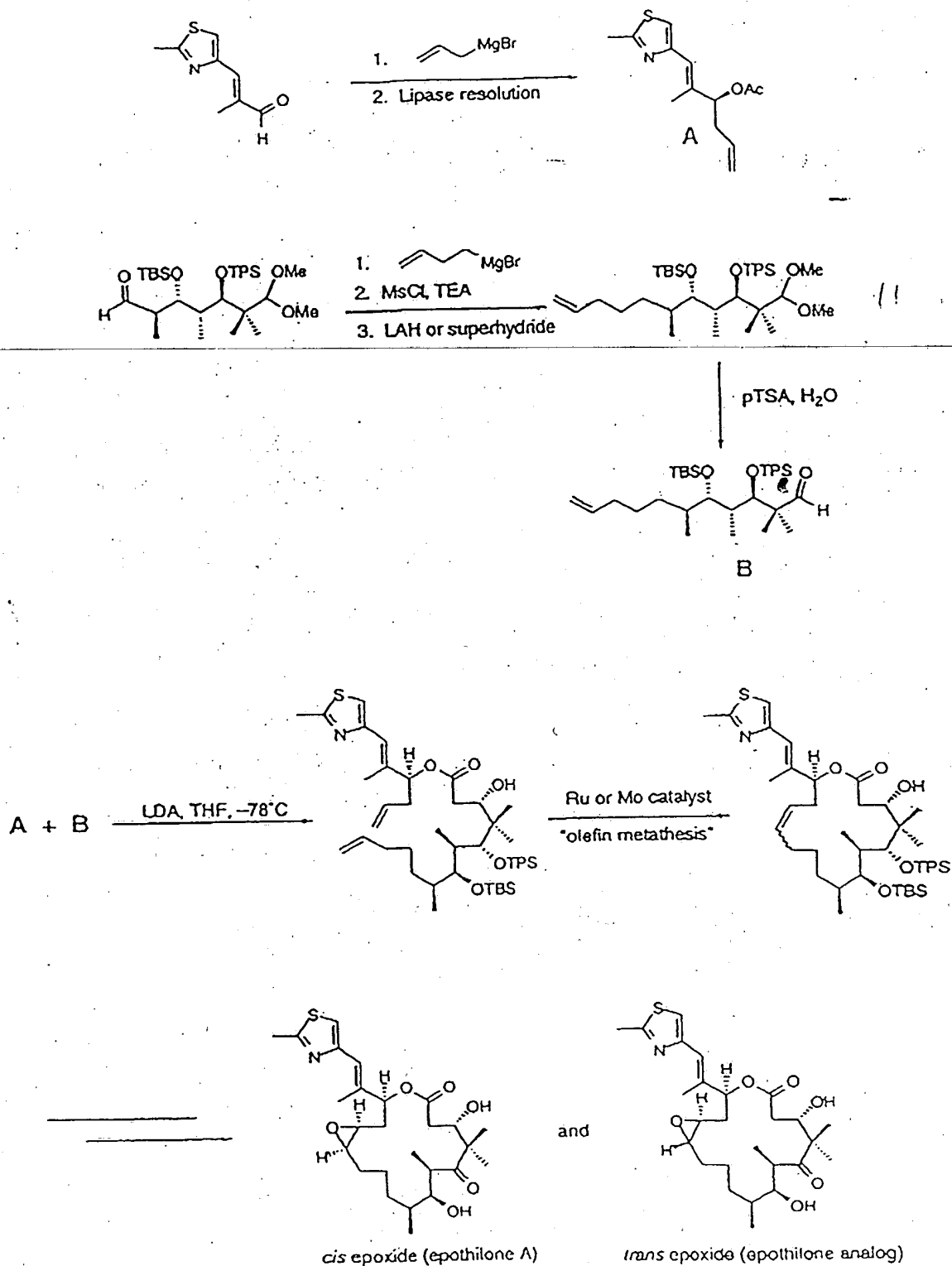
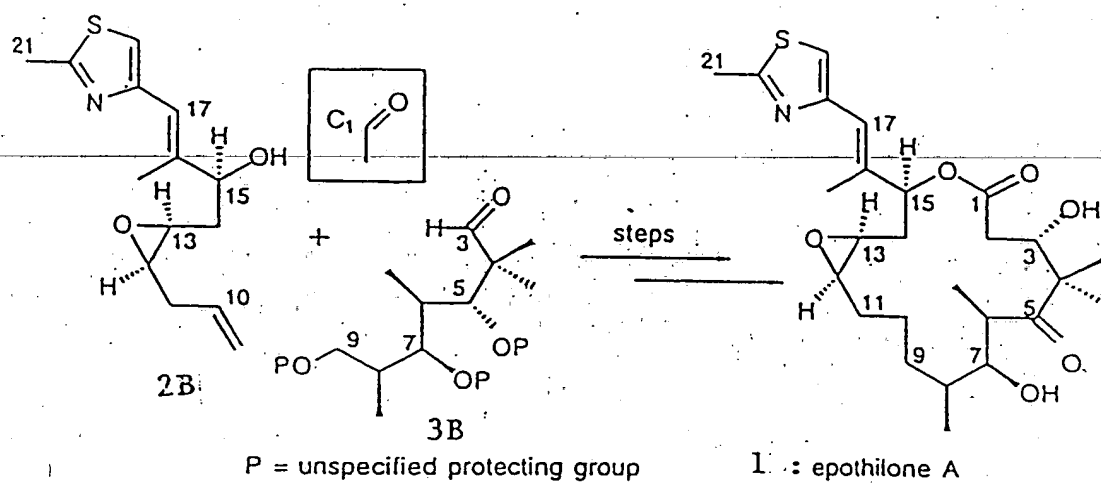


Figure 5

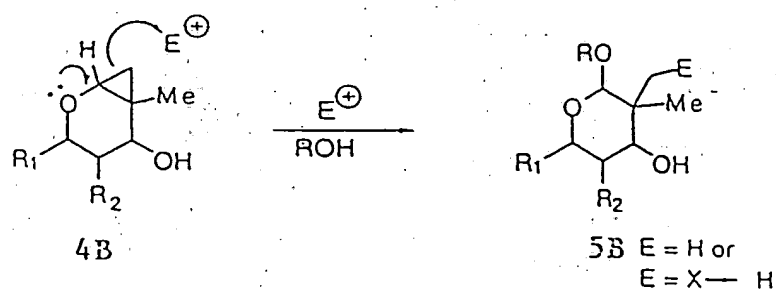


* 17 steps from known starting materials vs. 27 steps for aldol macrocyclization

Figure 6



Convergent strategy for a total synthesis of epothilone A (1).



The glycol cyclopropane solvolysis strategy for the introduction of geminal methyl groups.

Figure 7

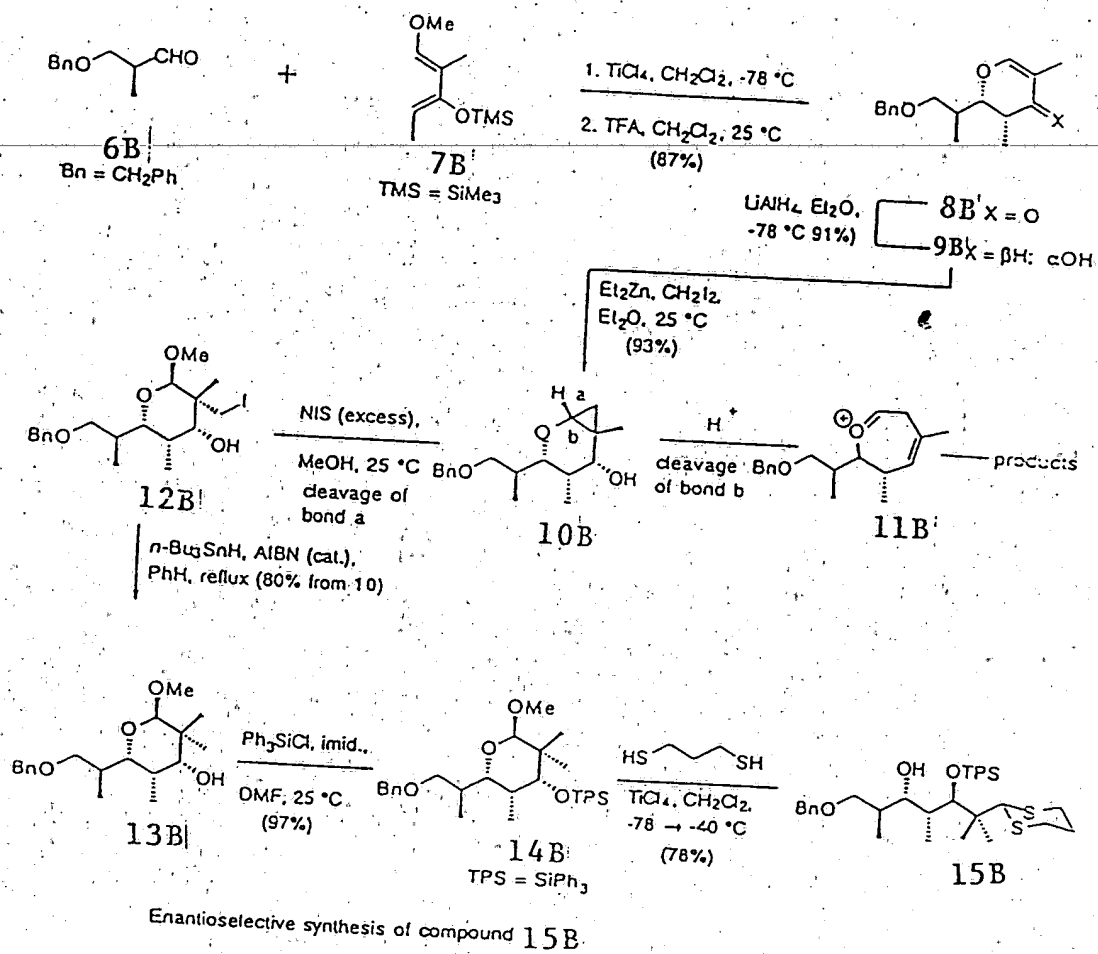
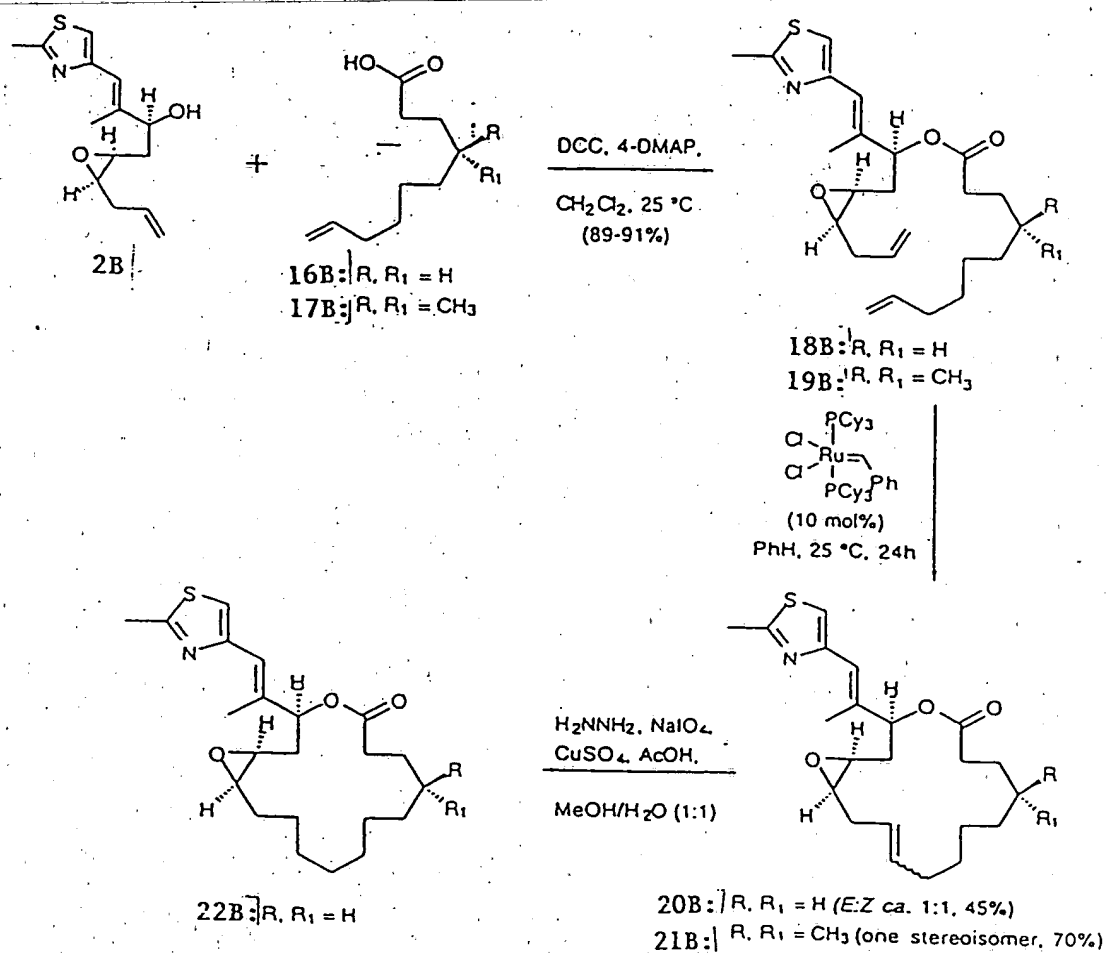


Figure 8



Construction of epothilone model systems 20^B, 21^B, and 22^B by ring-closing olefin metathesis

Figure 9

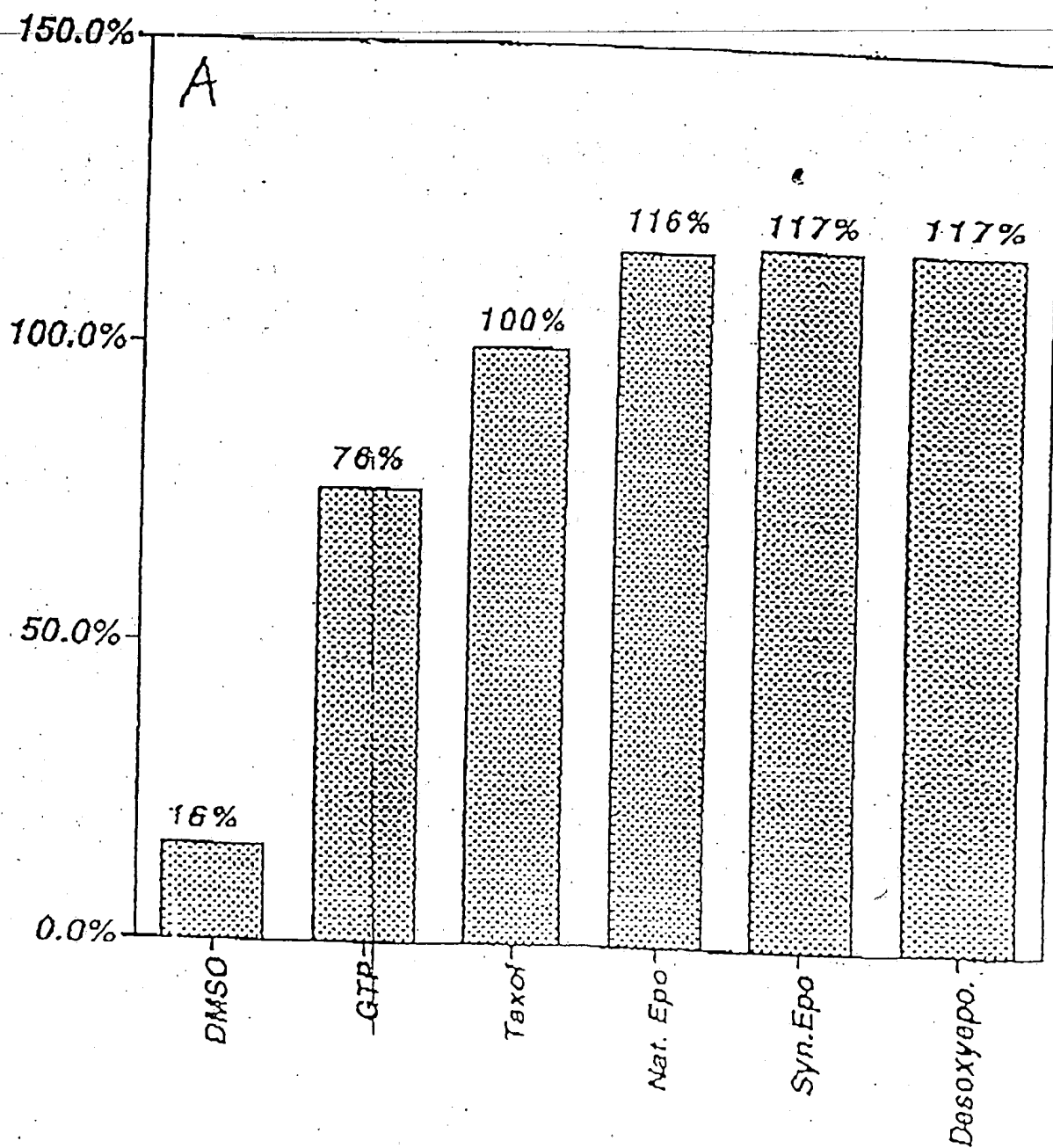


Figure 10

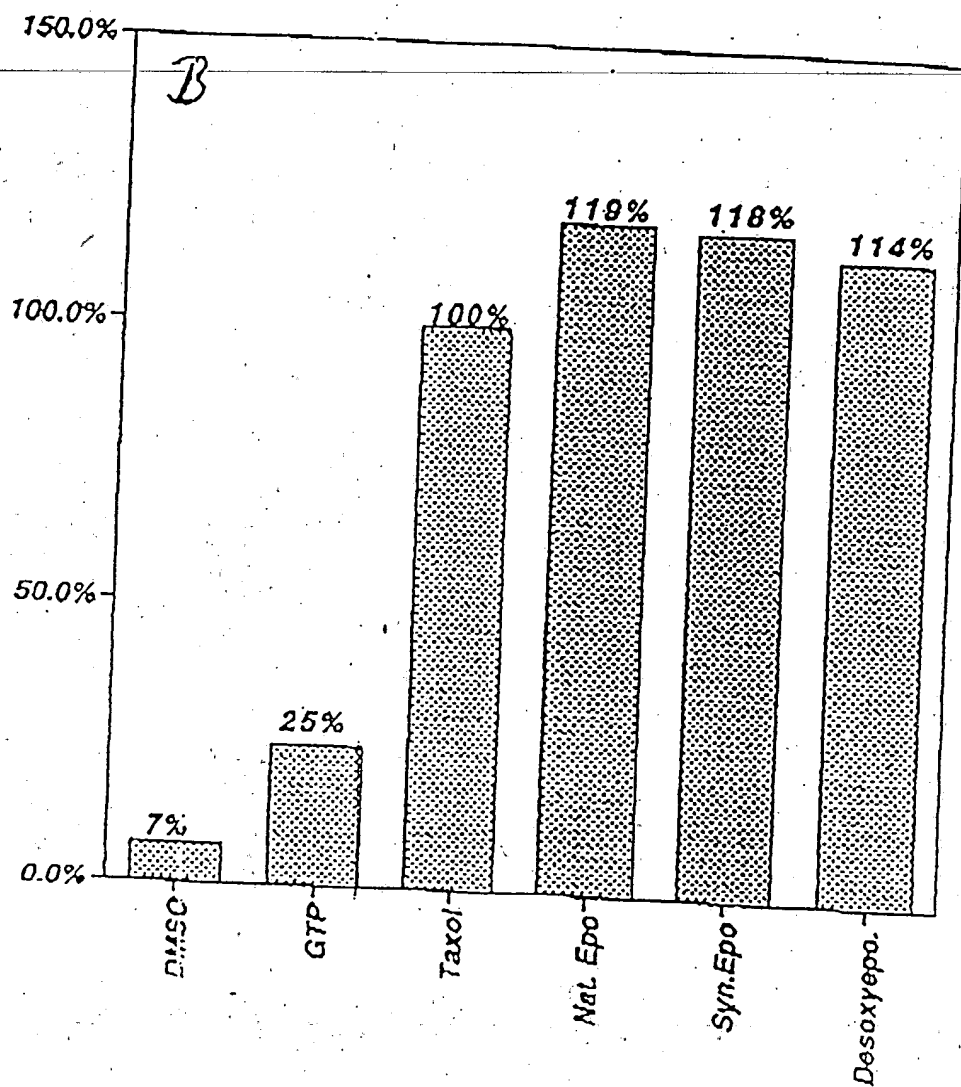
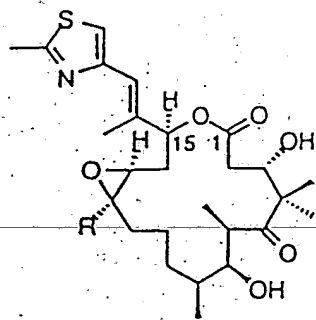


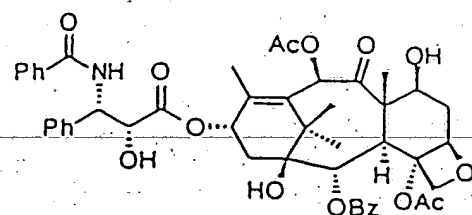
Figure 11

(A)



R = H; epothilone A
R = CH₃; epothilone B

(B)



1A: taxol™

Figure 12

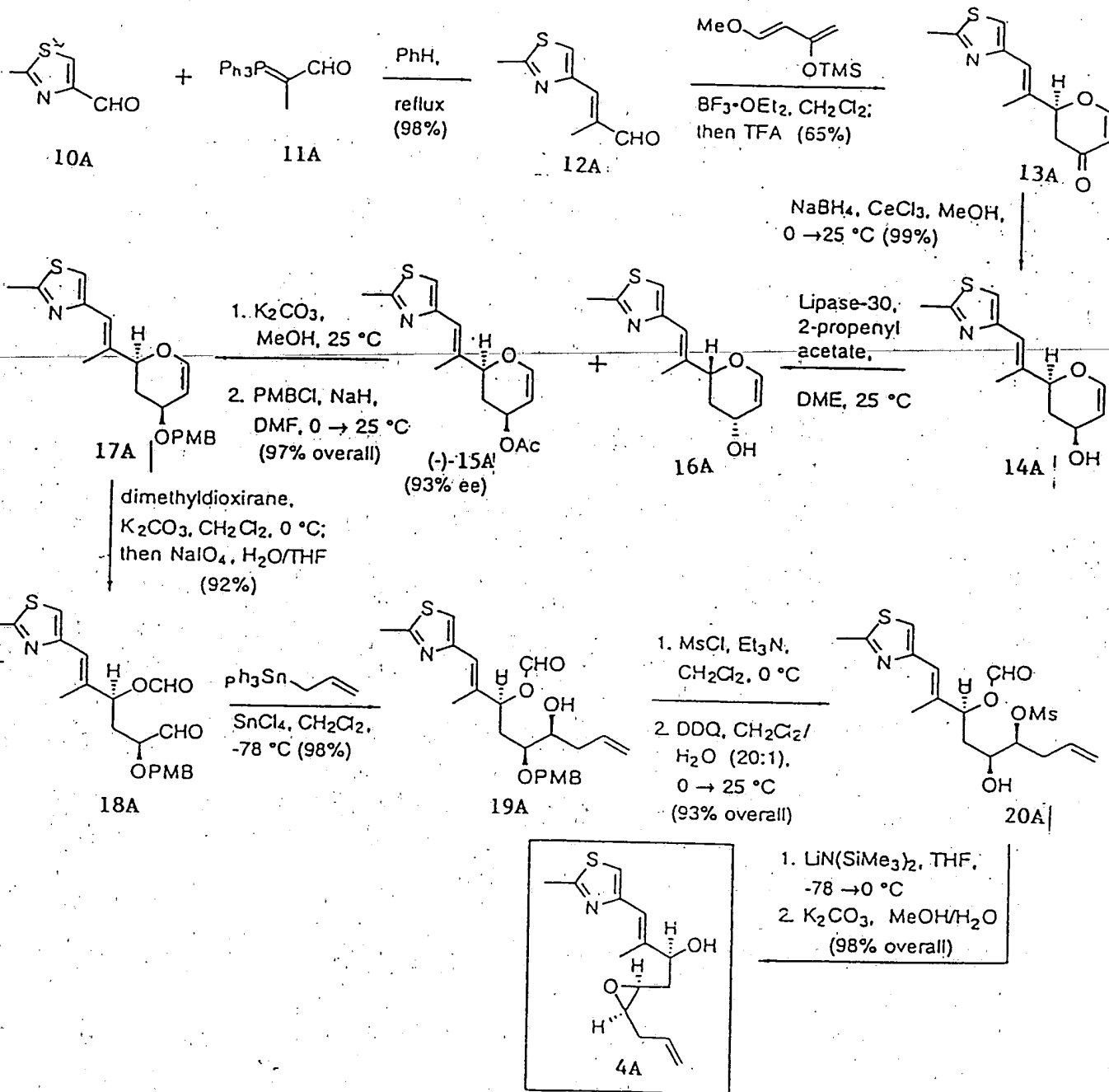


Figure 14

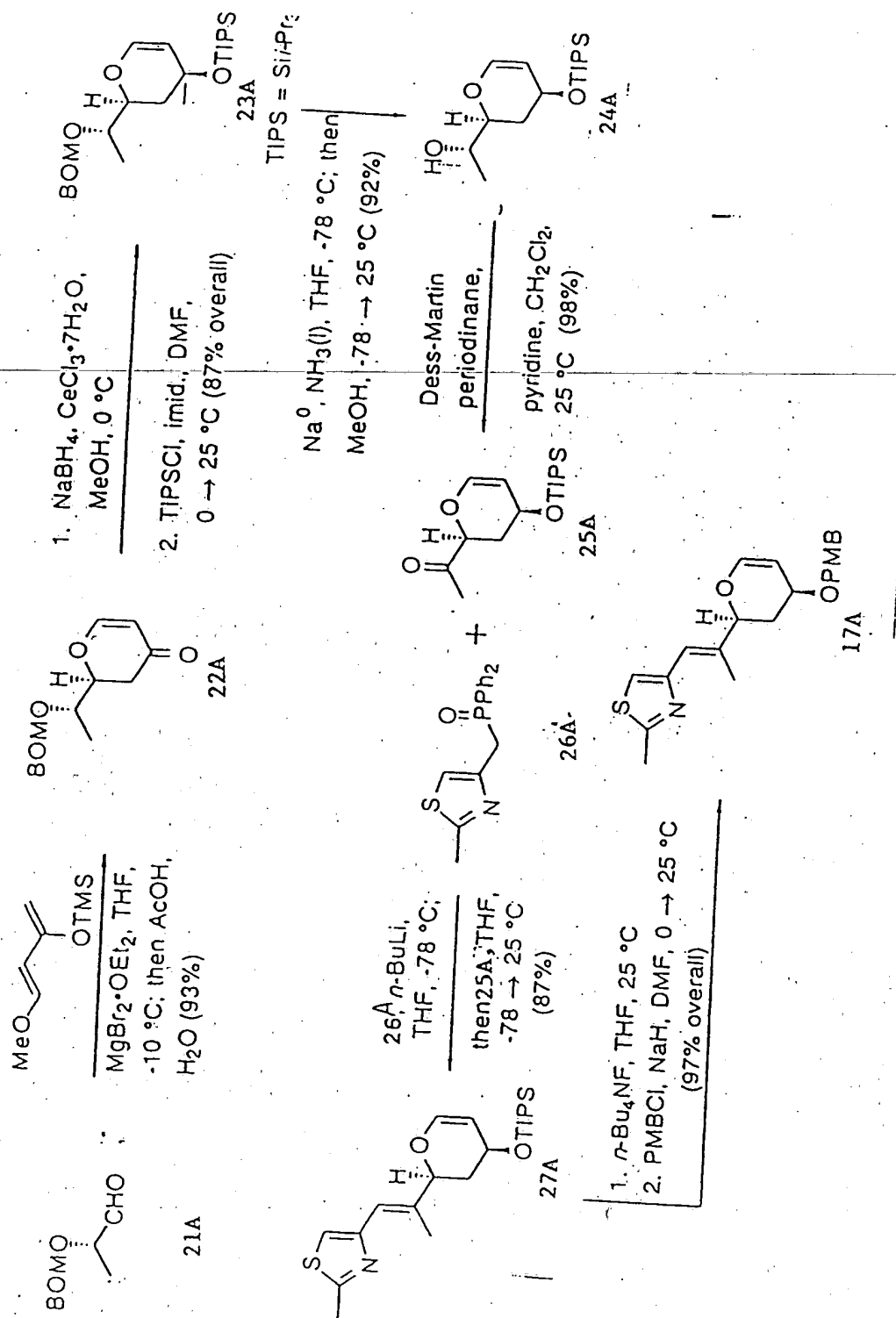


Figure 15

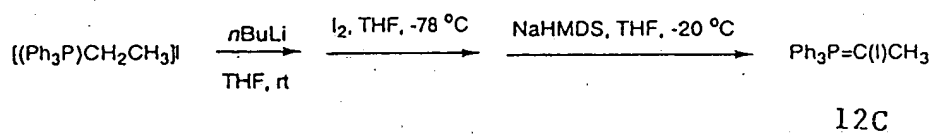
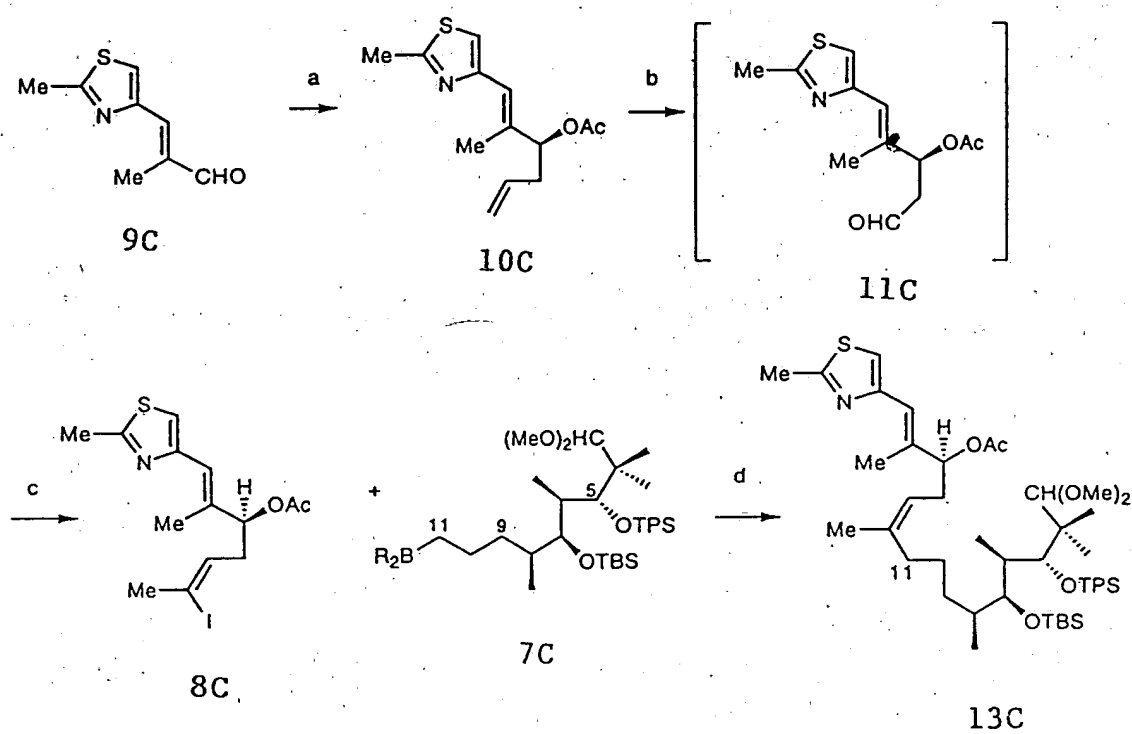


Figure 16

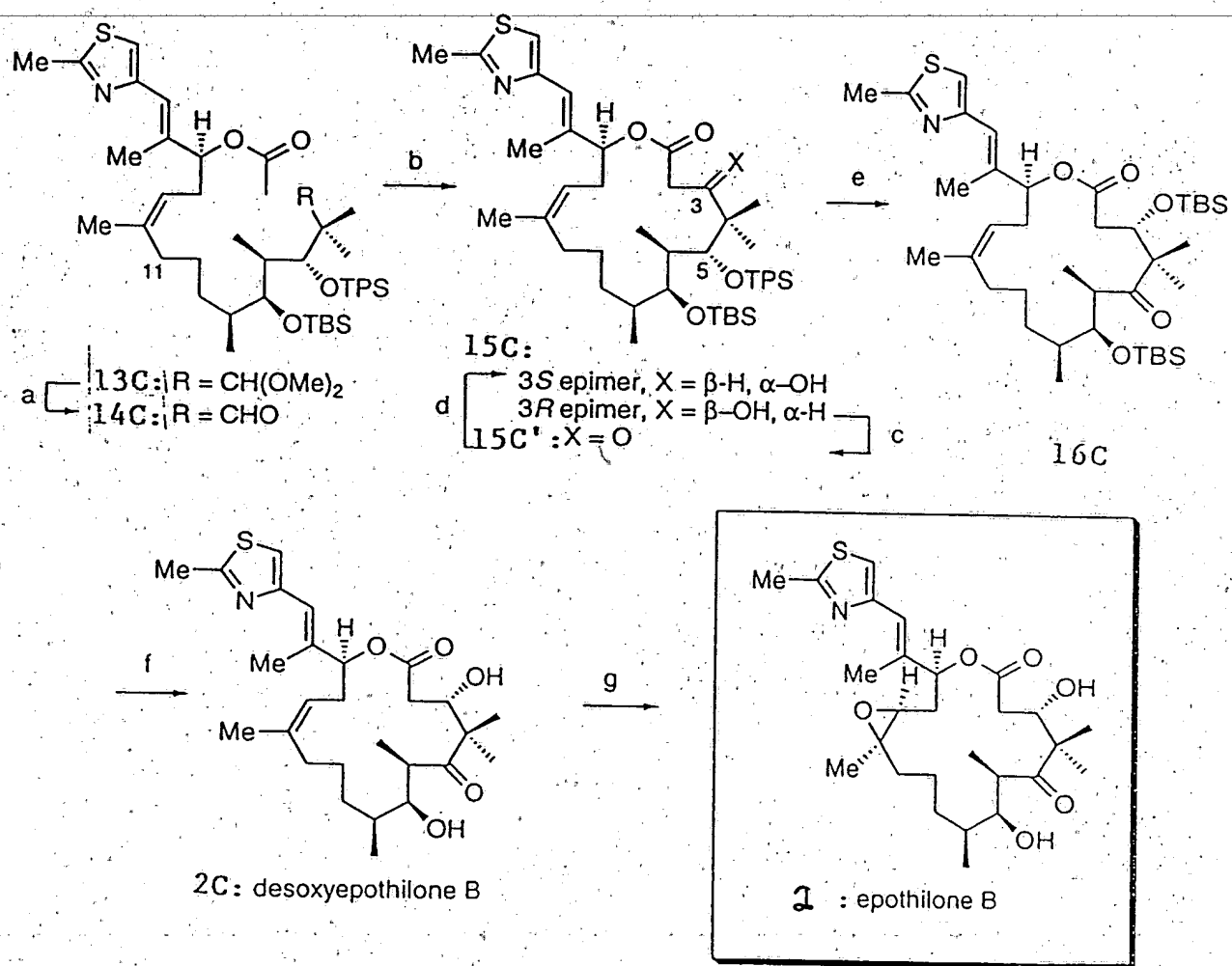


Figure 17

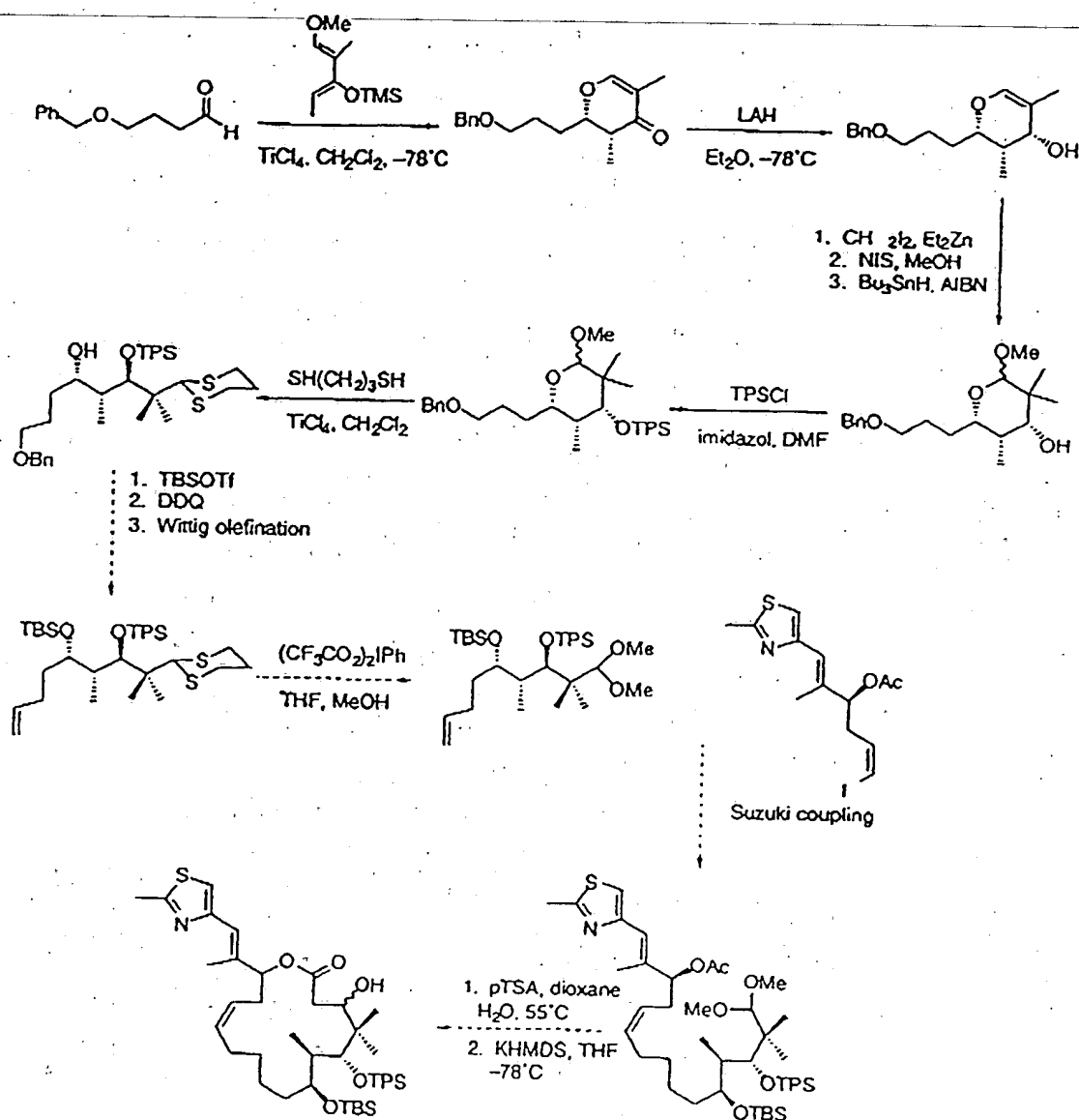


Figure 18

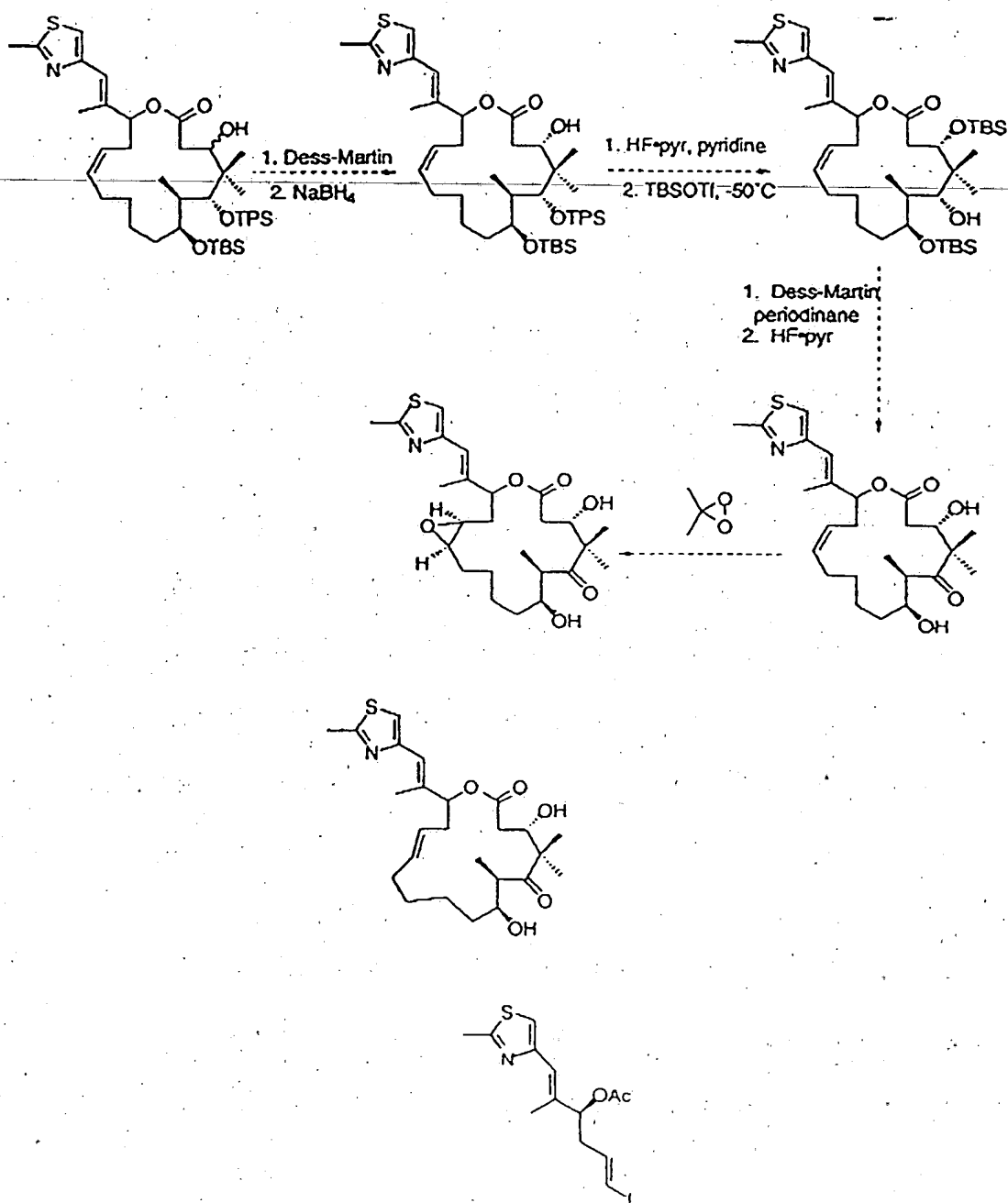


Figure 19

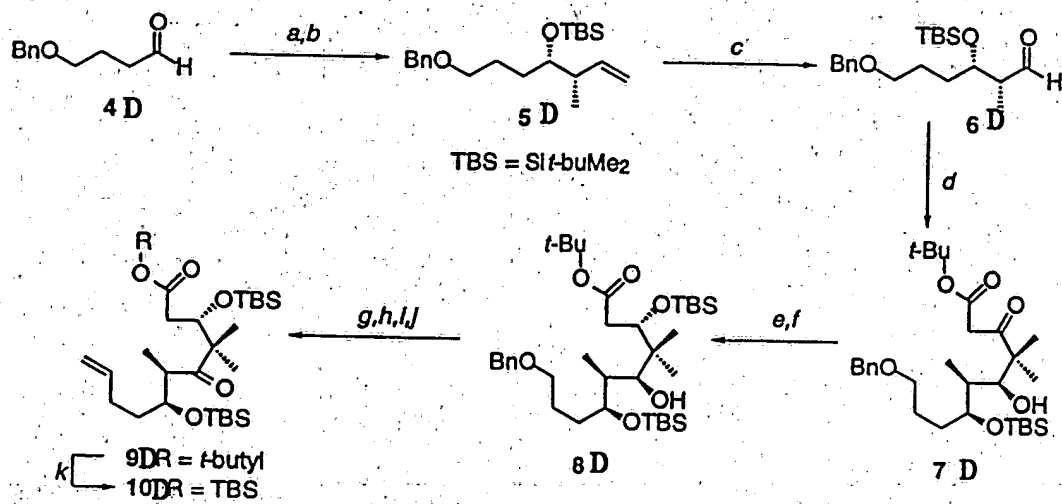
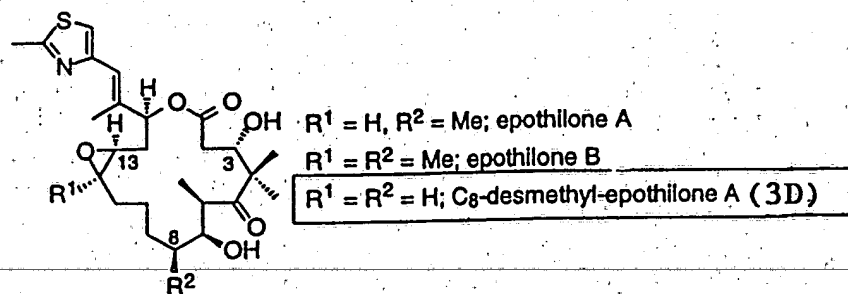


FIGURE 20

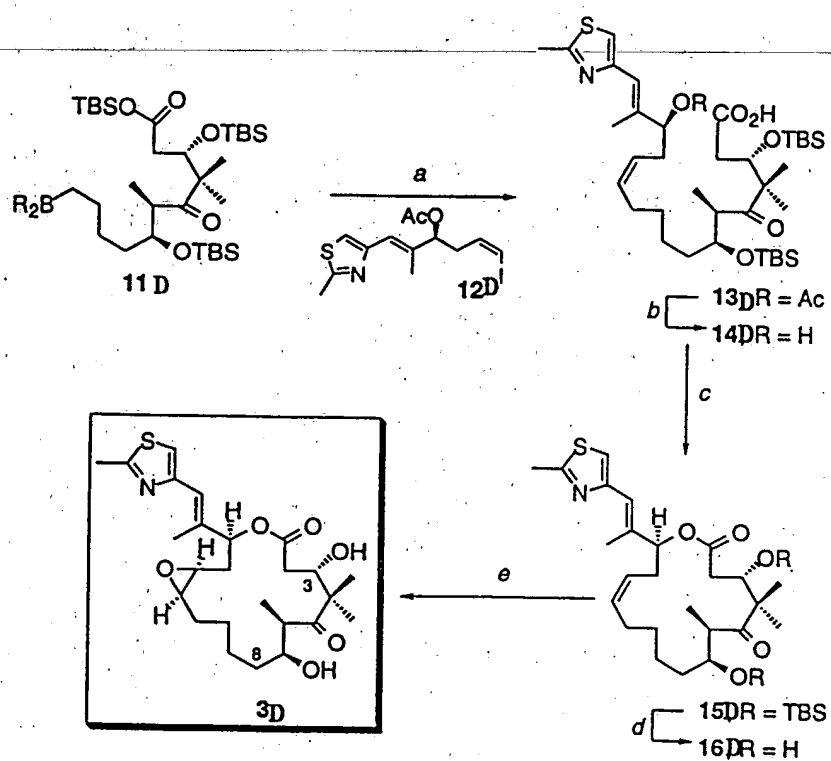


FIGURE 21

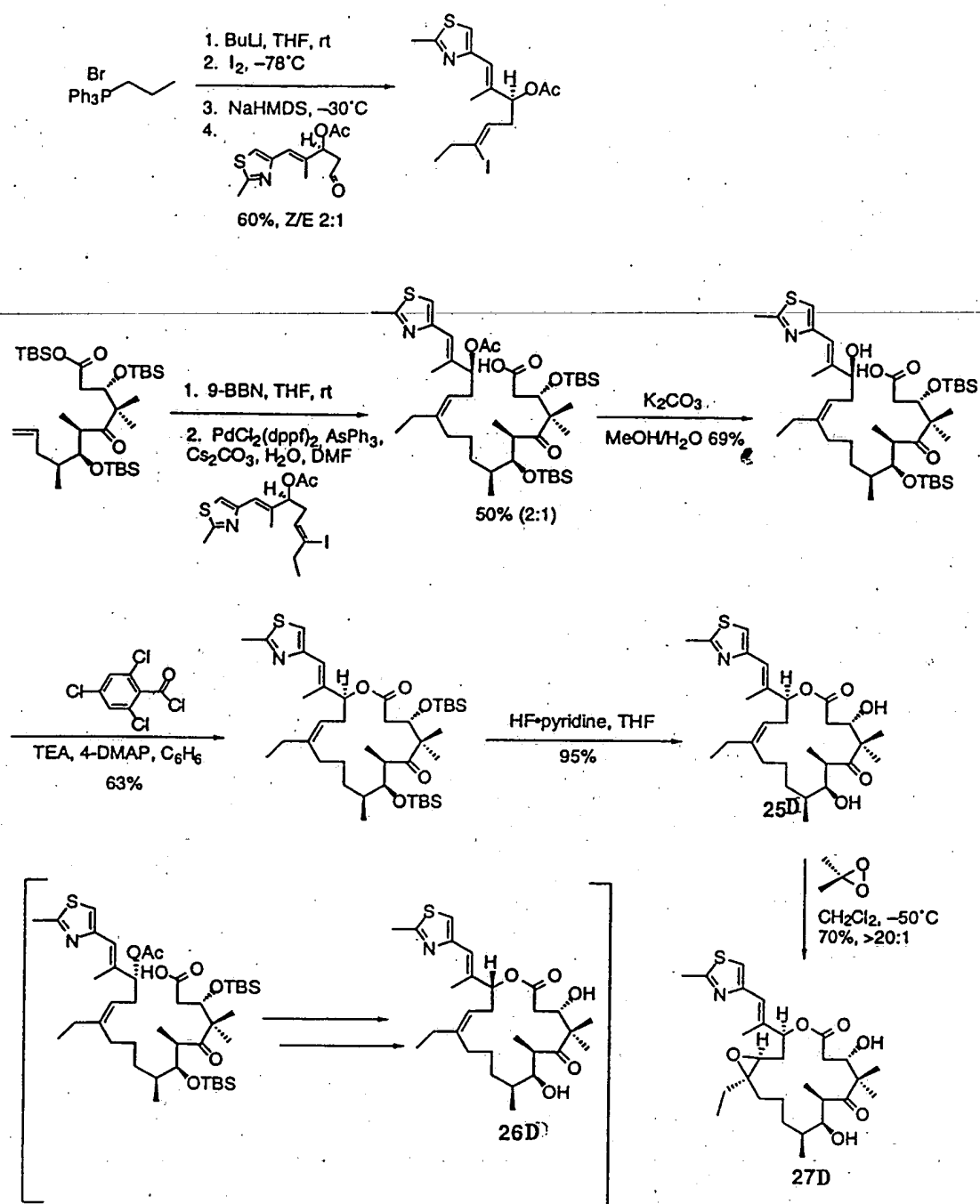


FIGURE 22

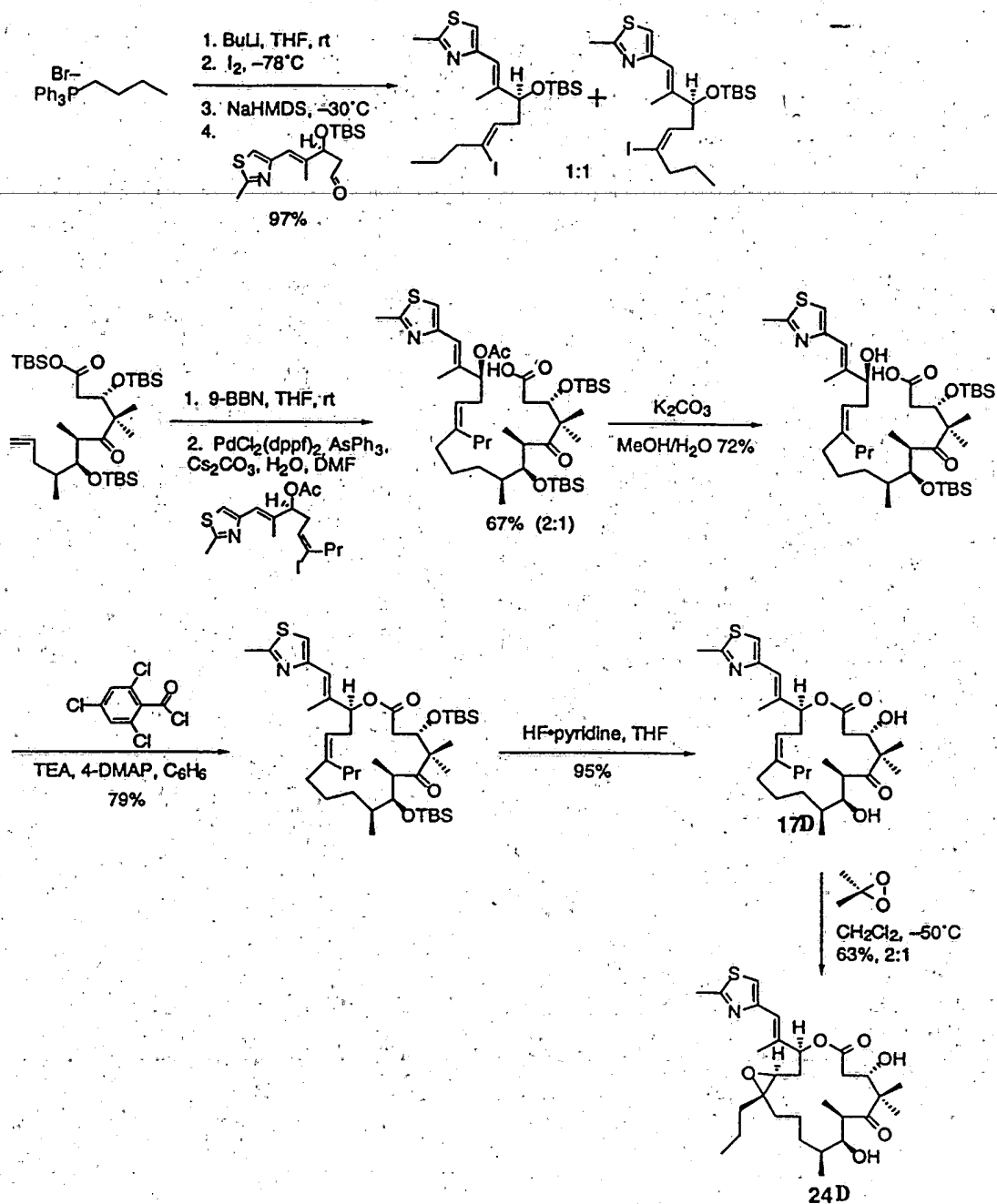


FIGURE 23

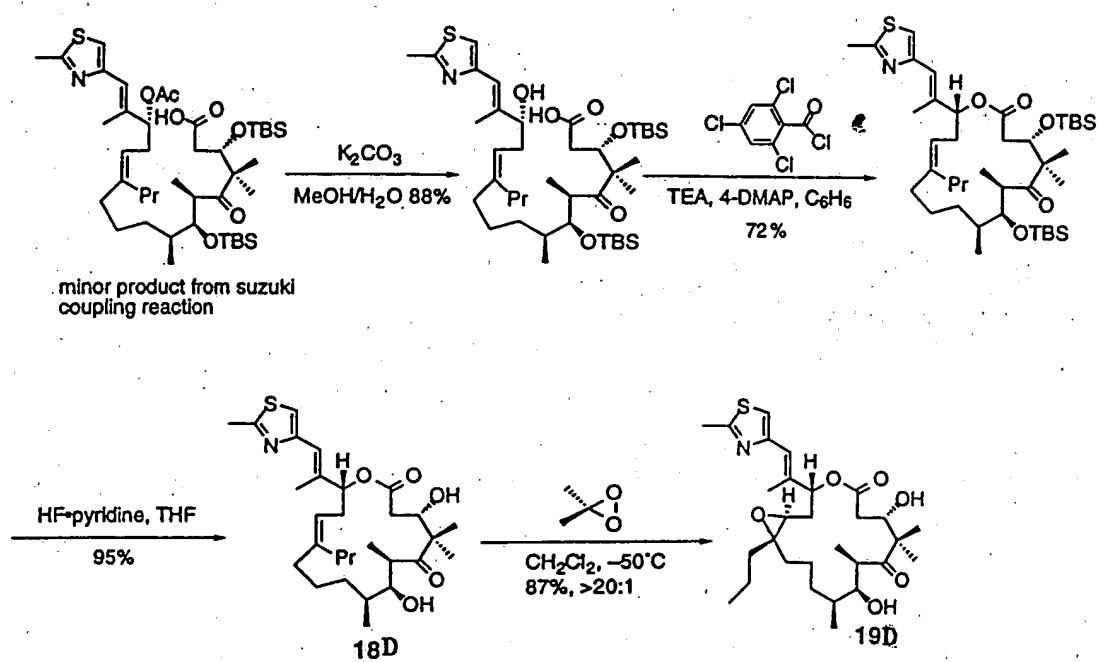


FIGURE 24

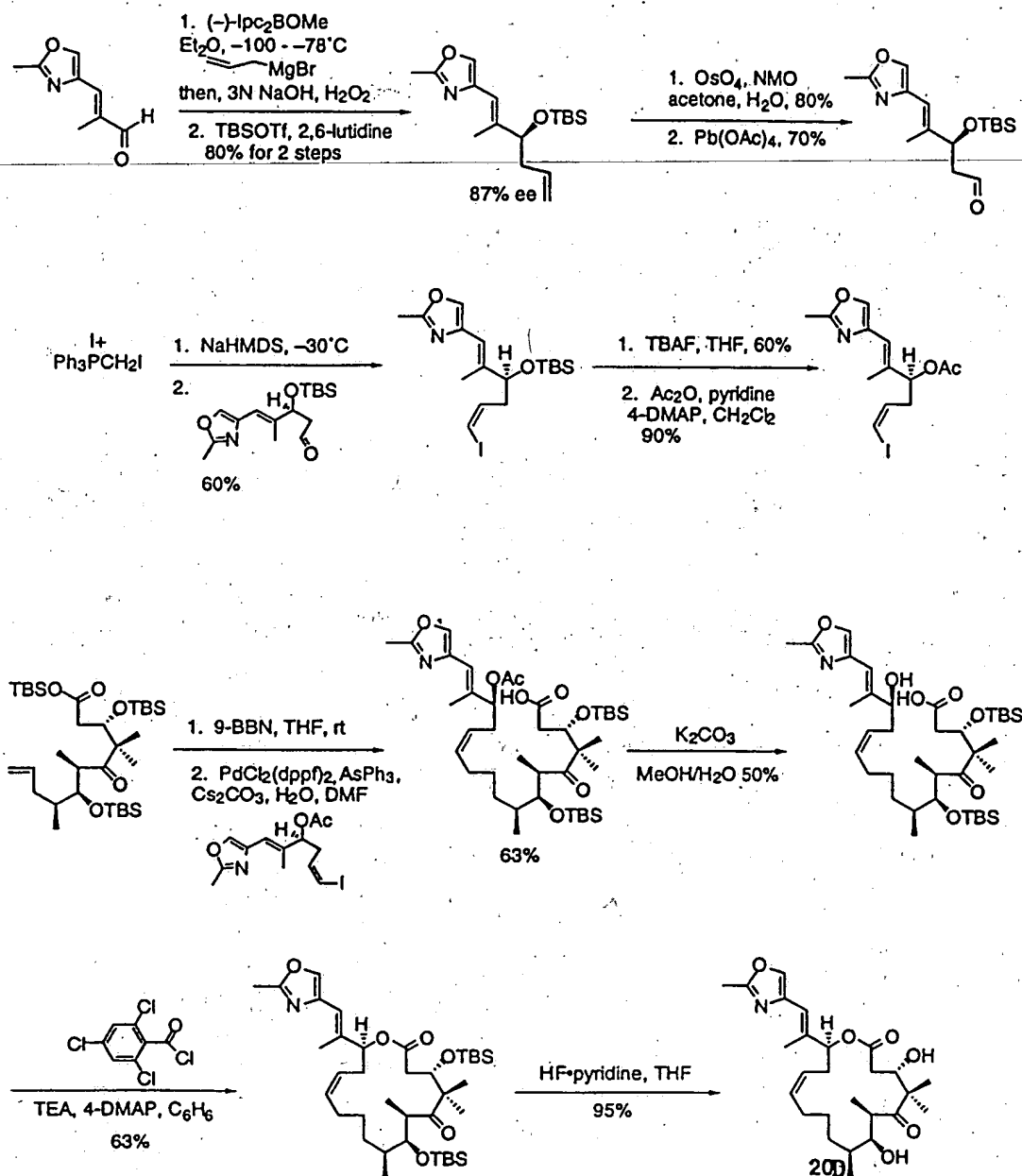


FIGURE 25

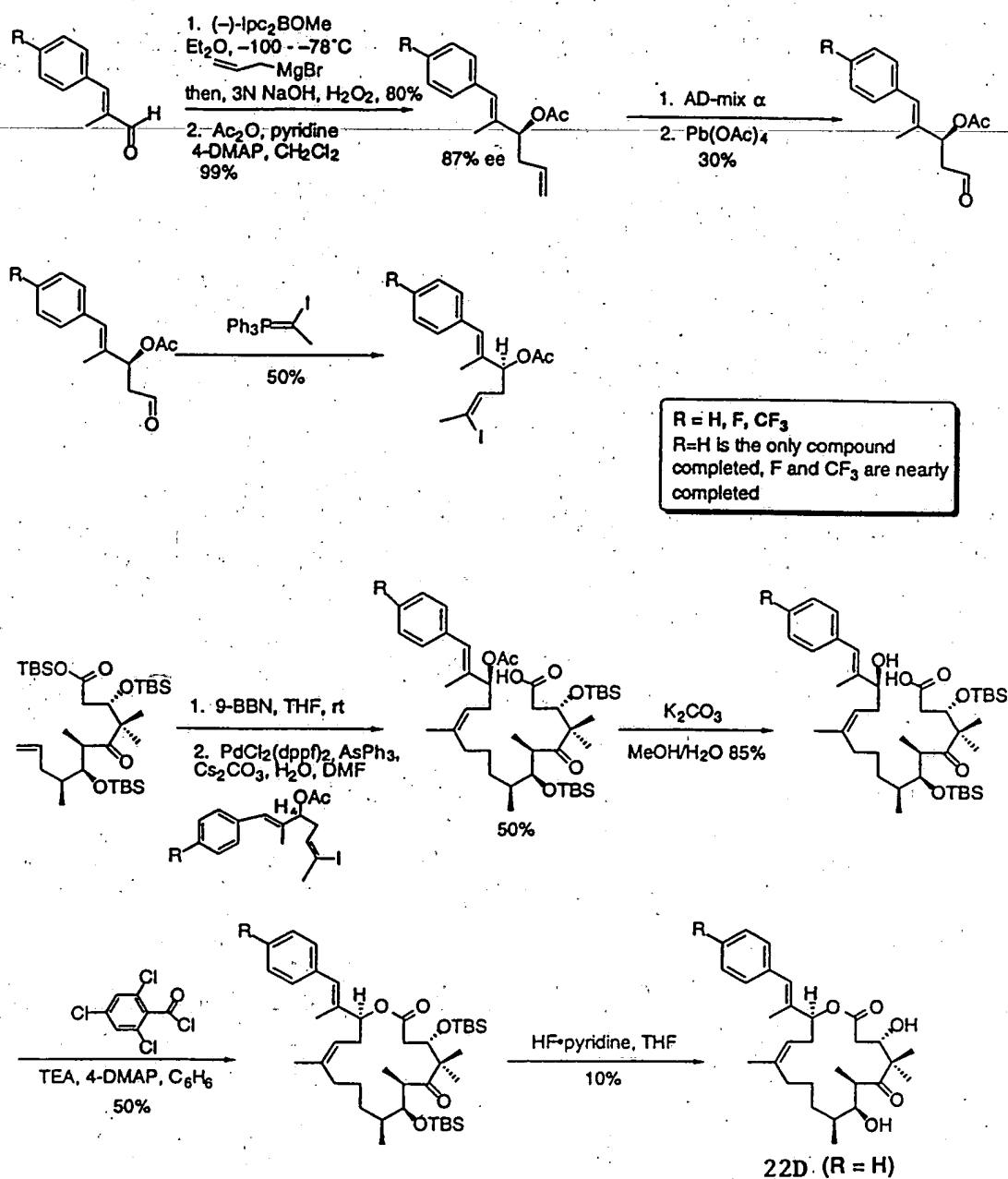


FIGURE 26

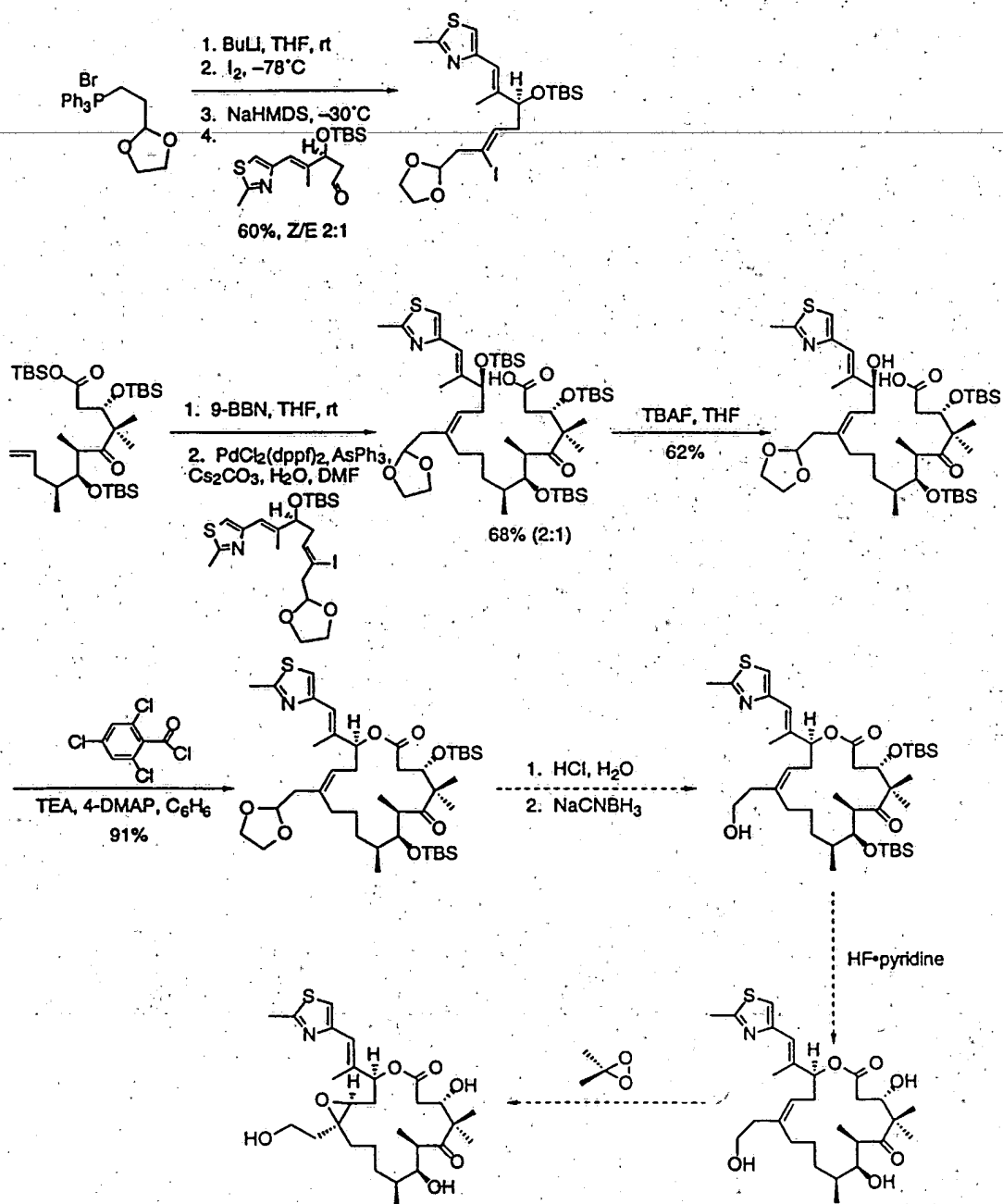


FIGURE 27

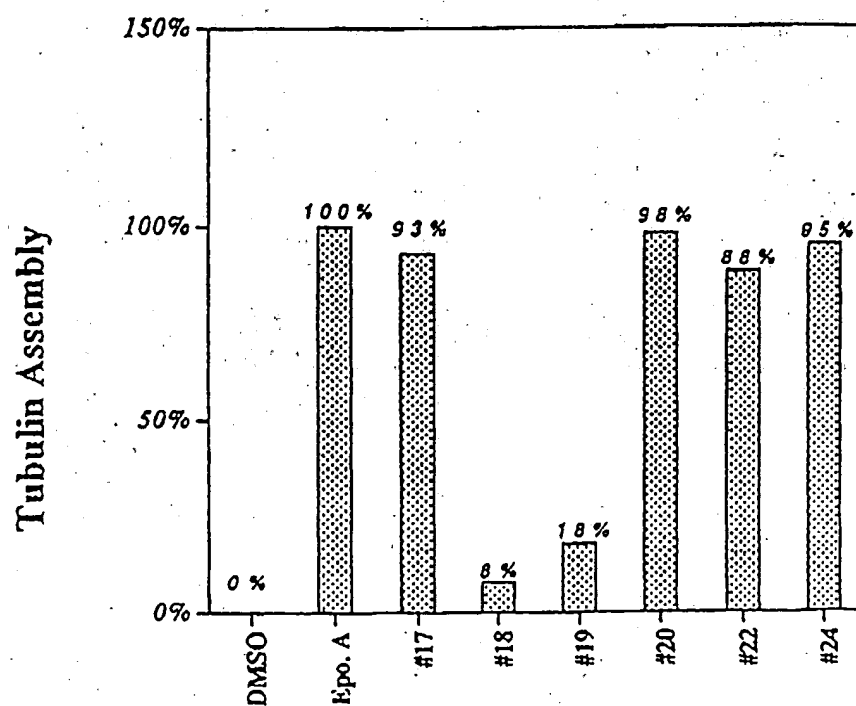
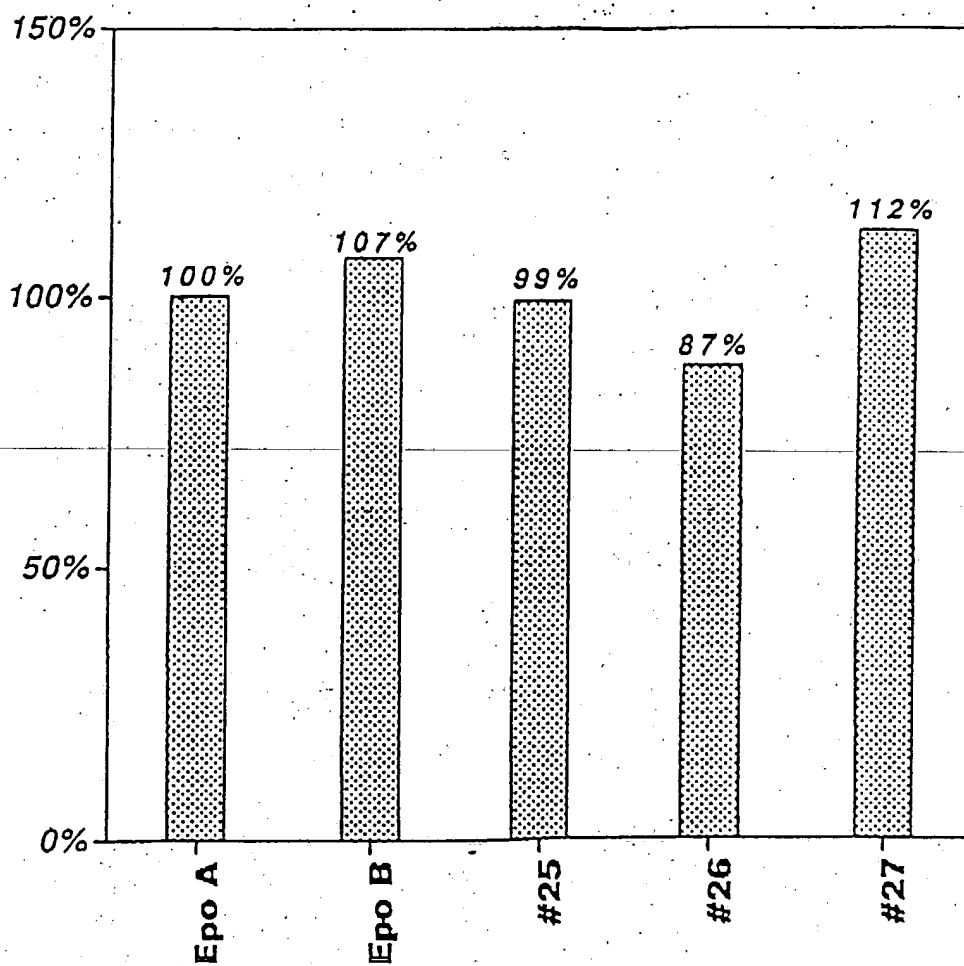


FIGURE 28

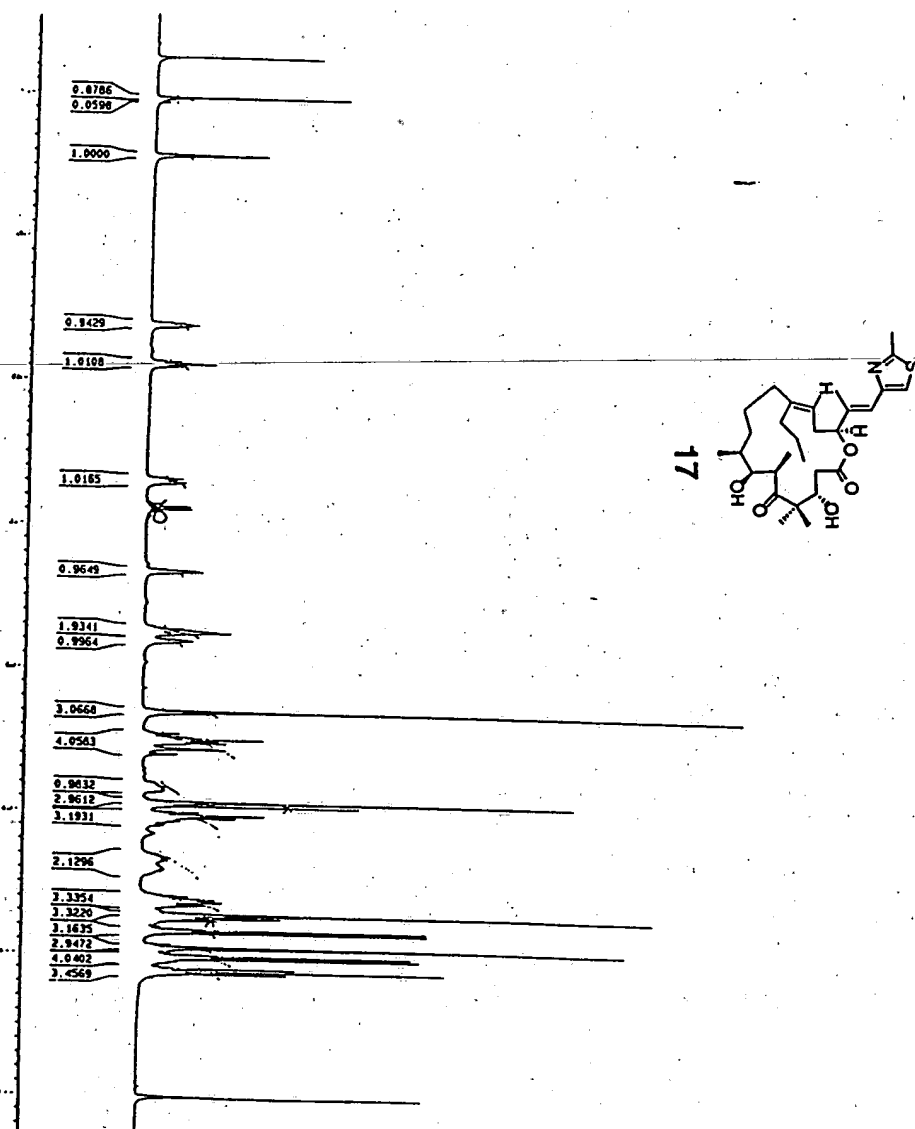


FIGURE 29

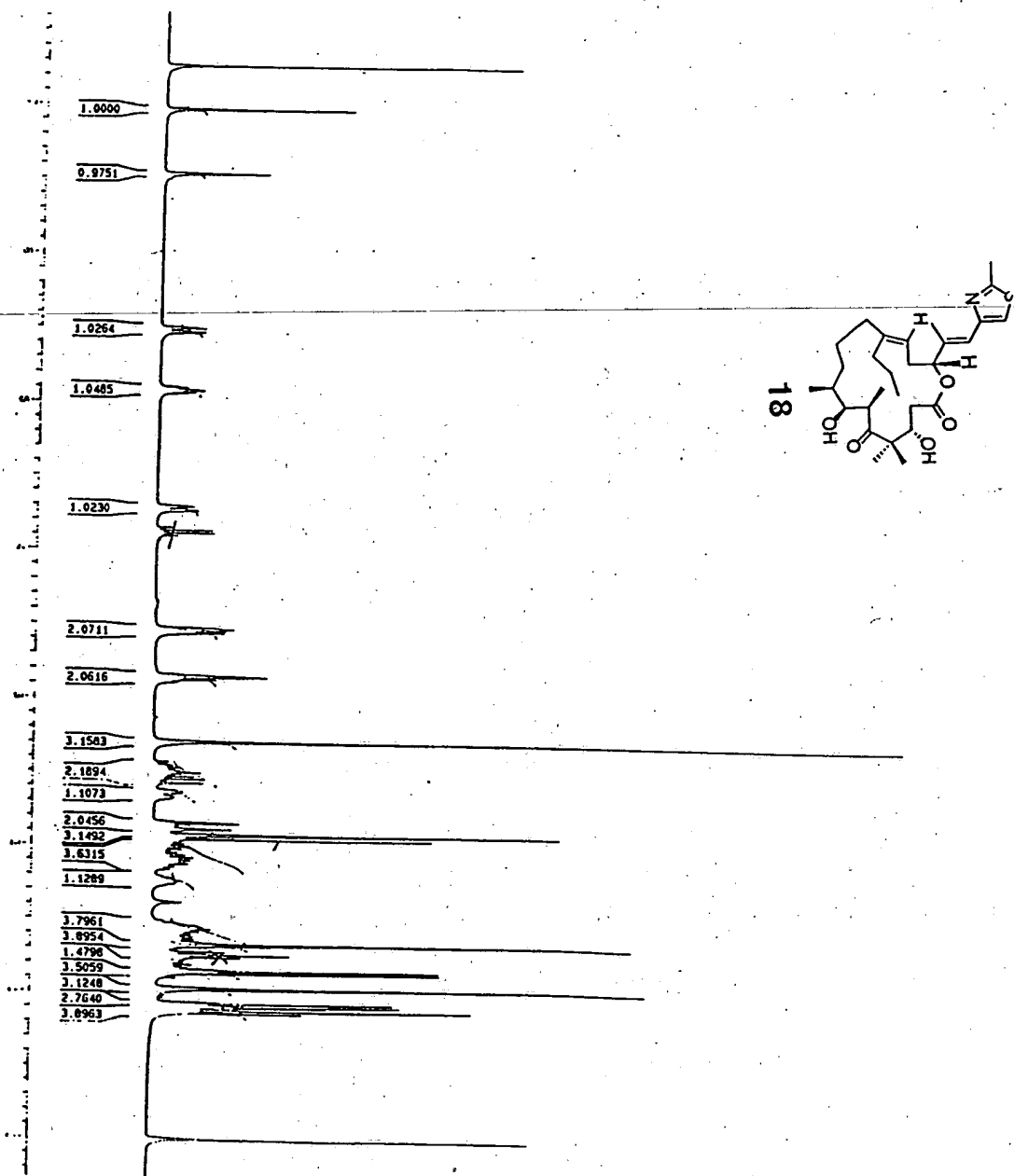


FIGURE \ 30

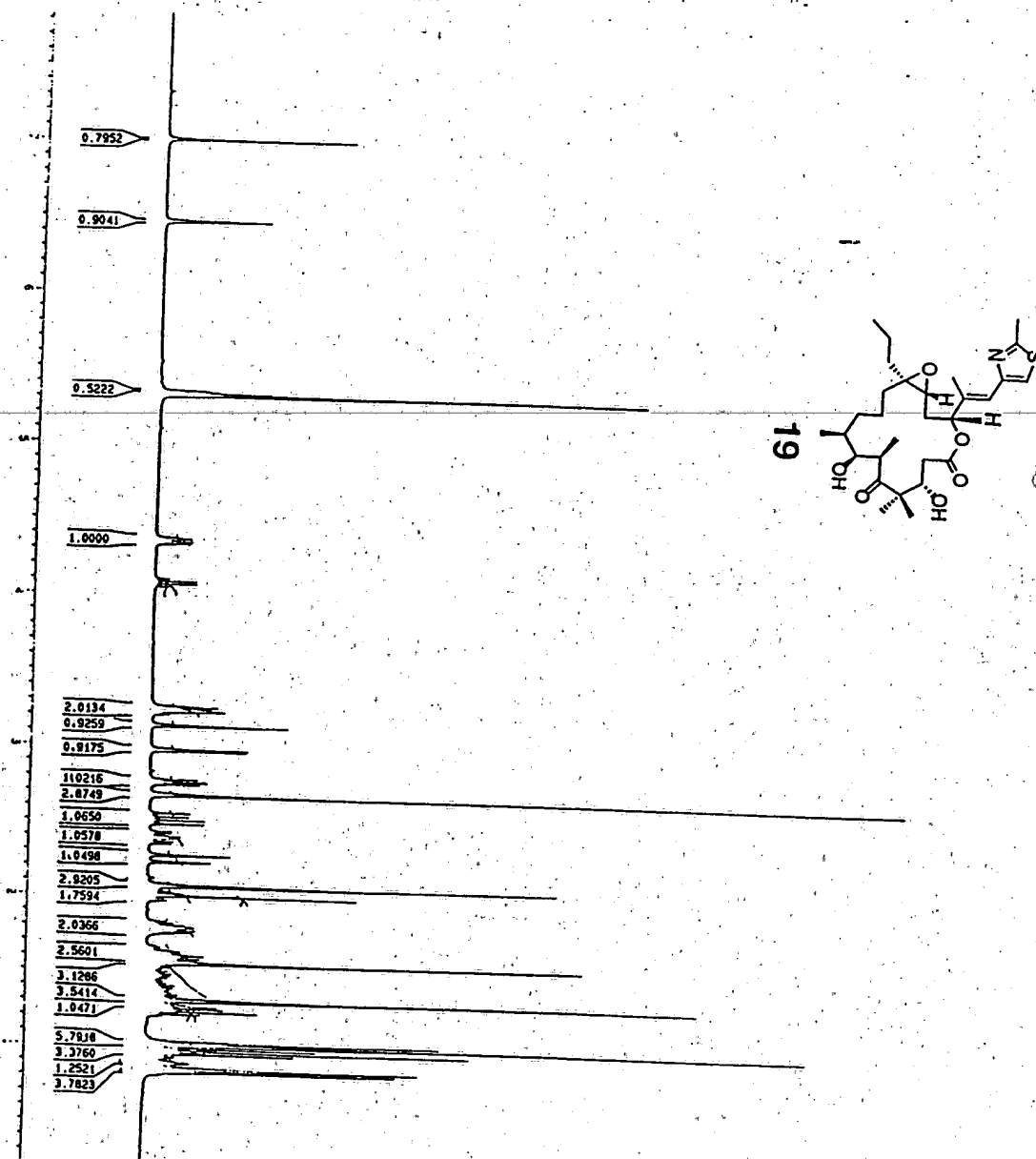


FIGURE 31

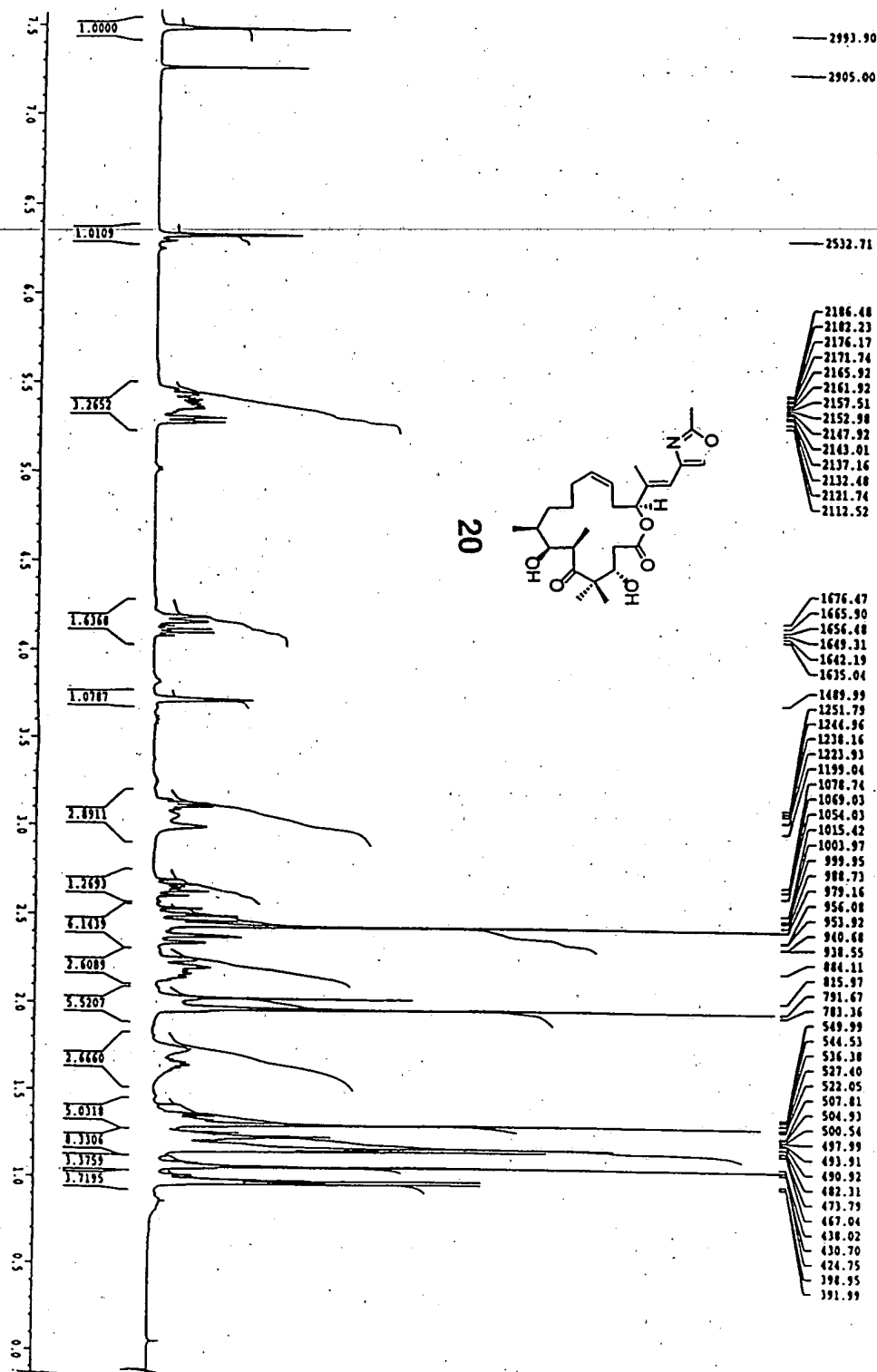


FIGURE 32

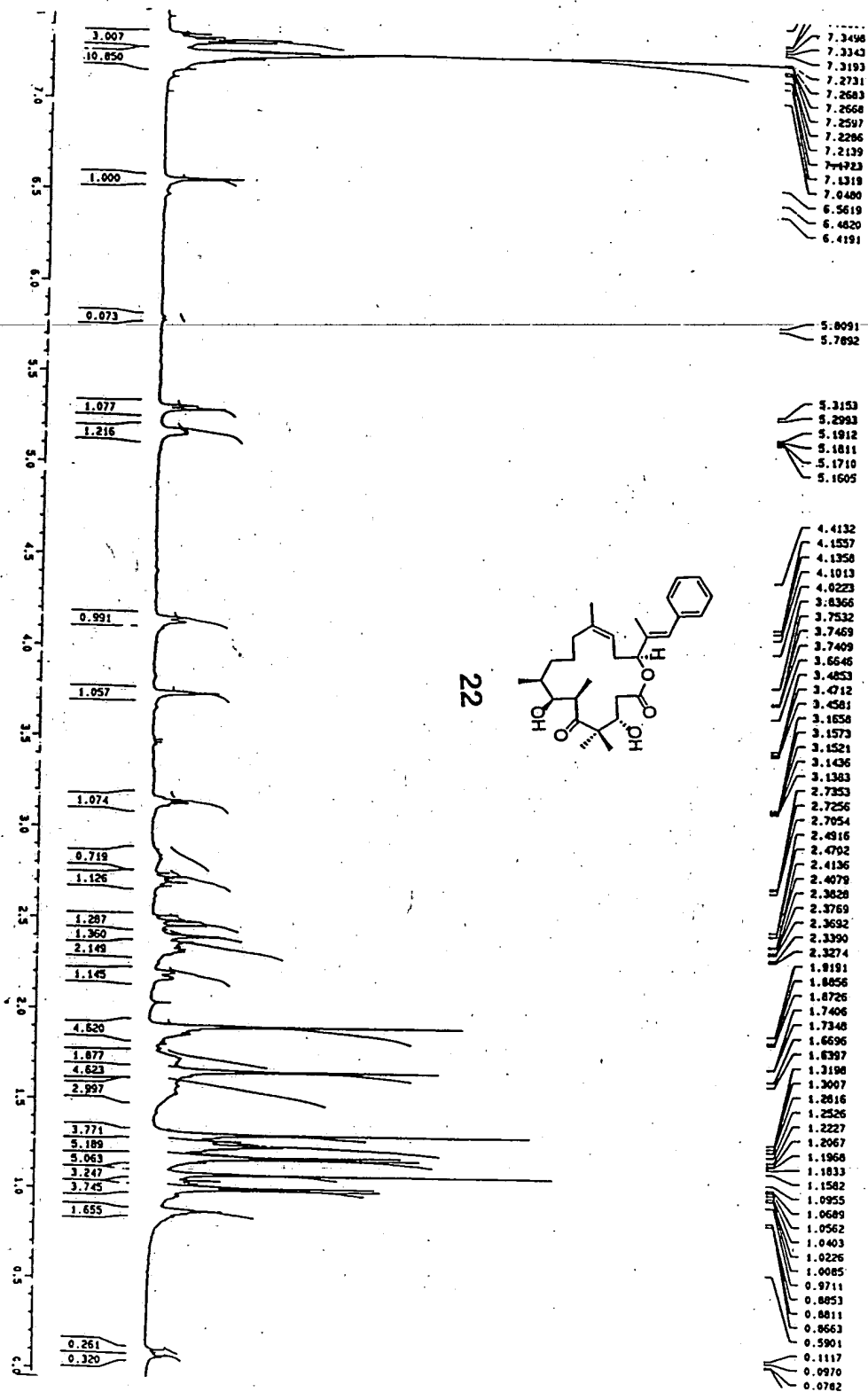


FIGURE 33

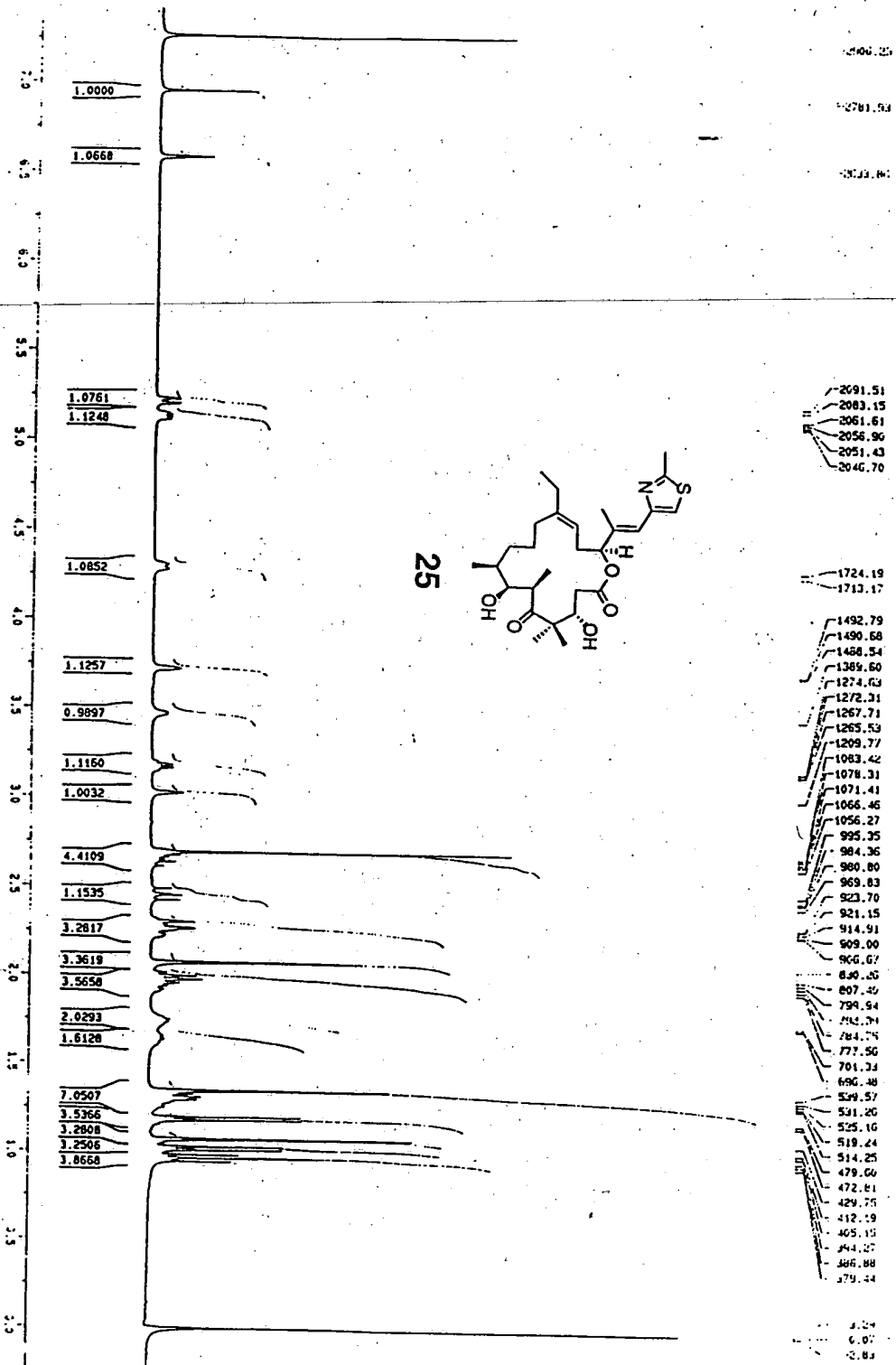
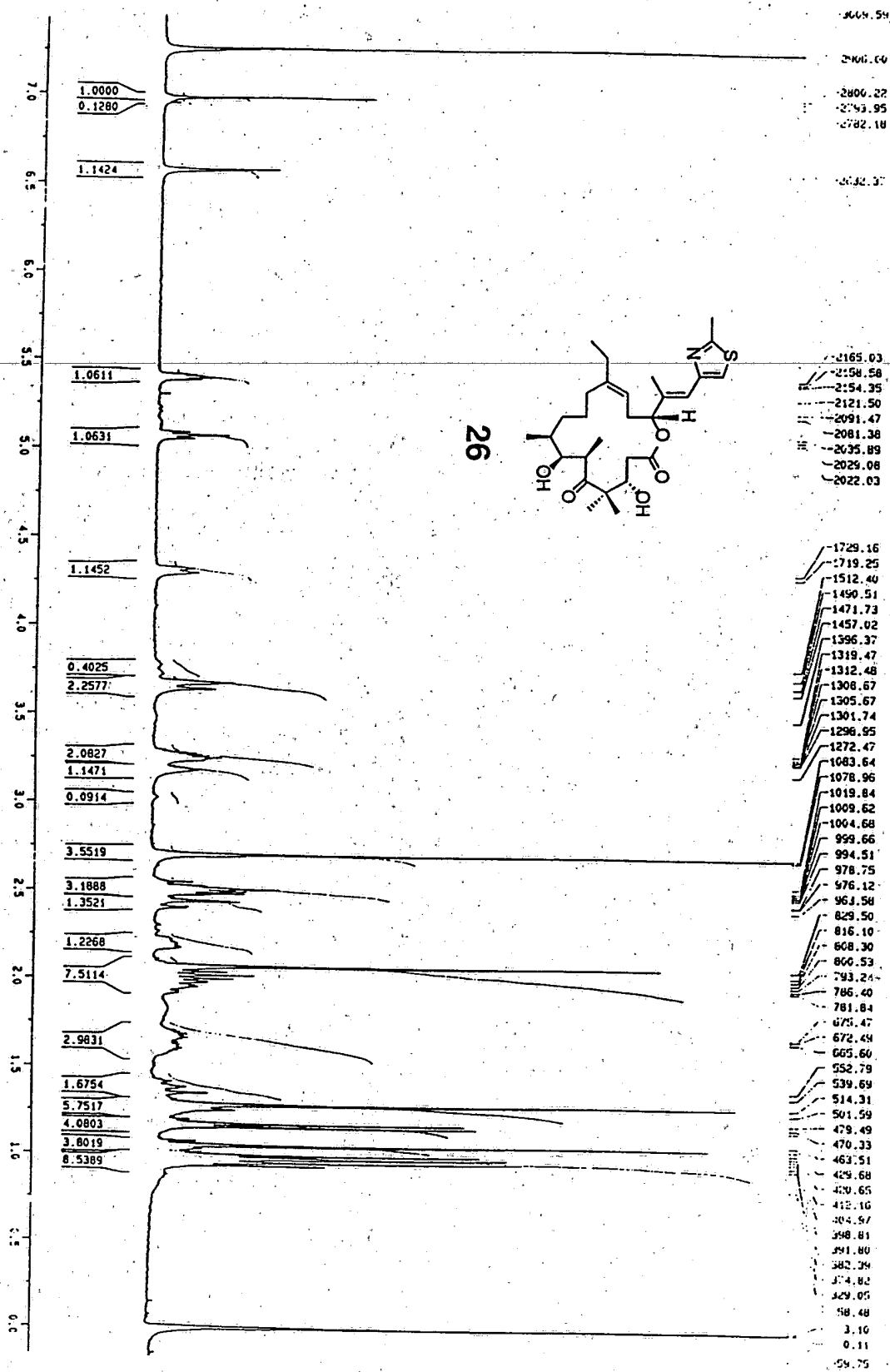


FIGURE 35



DSS-II-135-11

FIGURE 36



FIGURE 37

COMBINATION INDEX

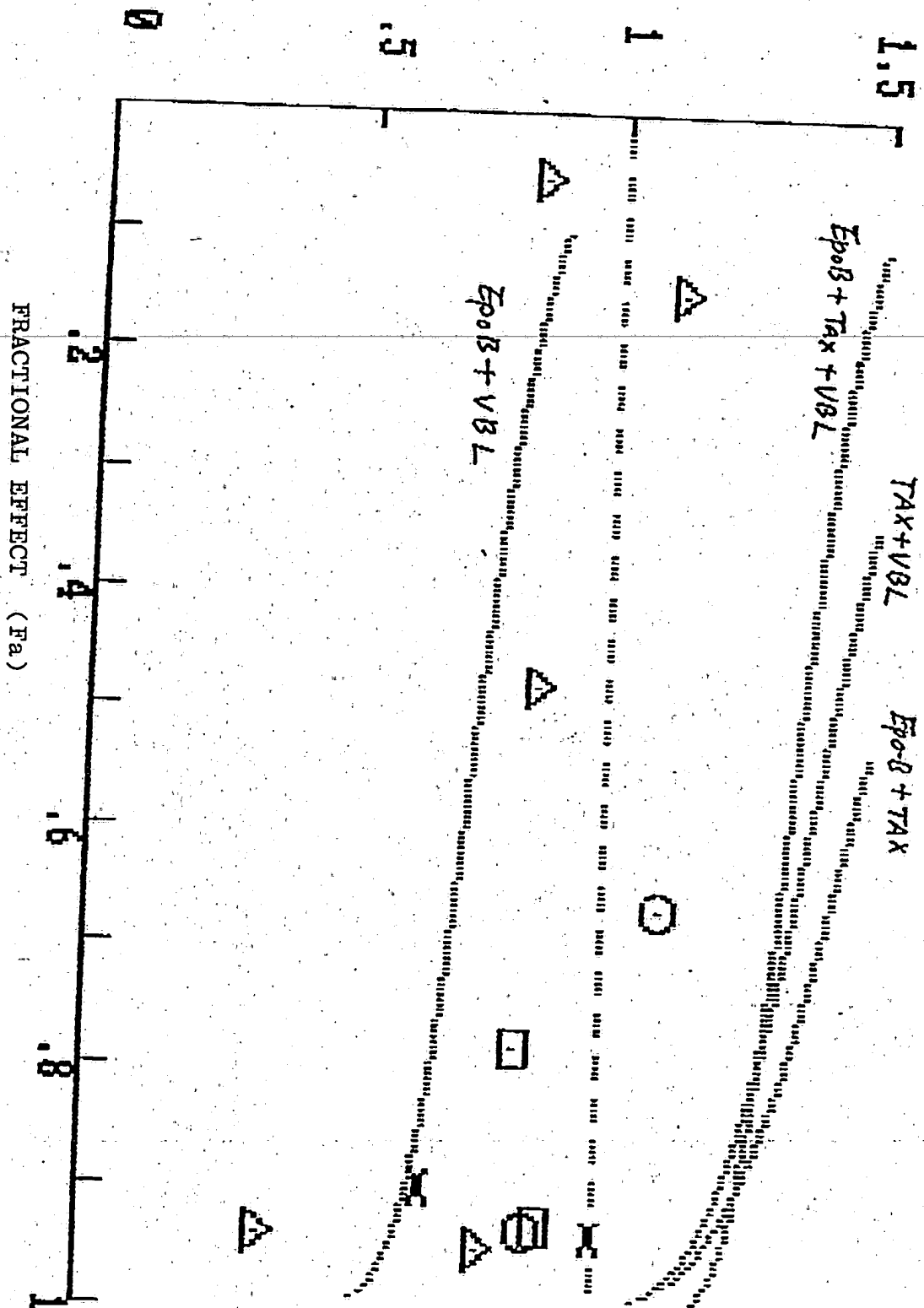
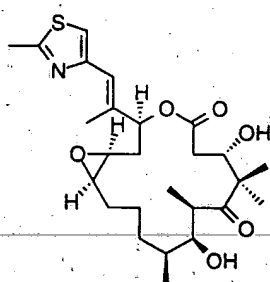
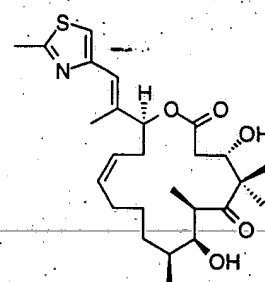


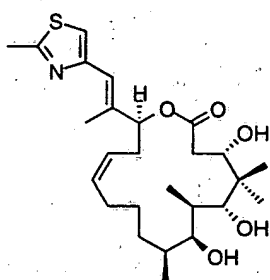
Figure 38



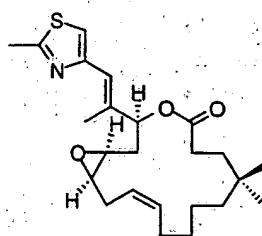
epothilone A
(0.0027)
[0.020]



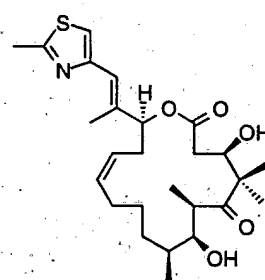
desoxyepothilone A
1
(0.022)
[0.012]



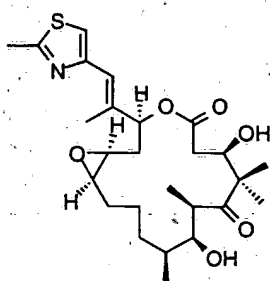
2
(14.23)
[6.28]



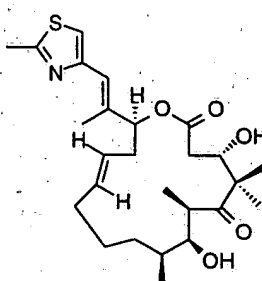
3
(271.1)
[22.4]



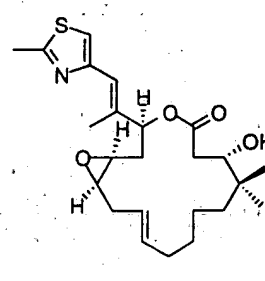
4
(2.12)
[43.0]



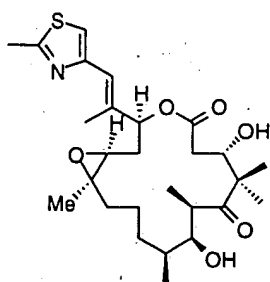
5
(>20)
[35.2]



6
(0.052)
[0.035]



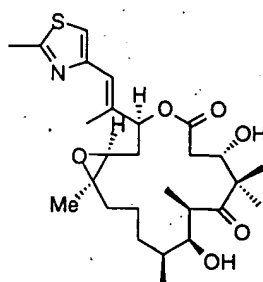
7
(7.36)
[9.82]



synthetic epothilone B

8

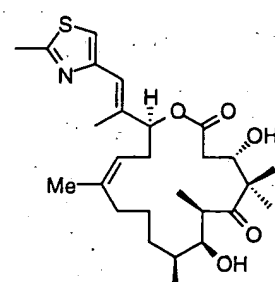
(0.00044)
[0.0026]



natural epothilone B

9

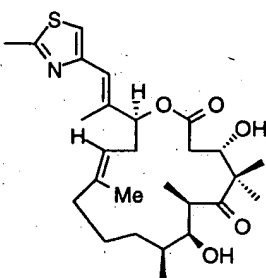
(0.00017)
[0.0012]



desoxyepothilone B

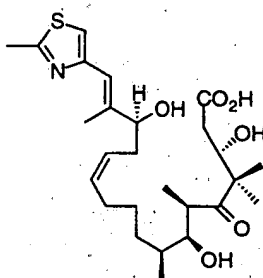
10

(0.0095)
[0.017]



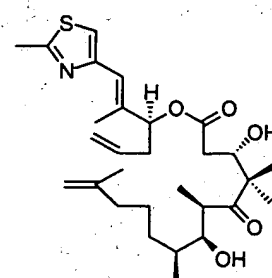
11

(0.090)
[0.262]



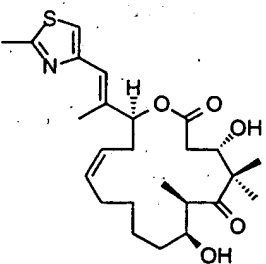
12

(0.79)
[>5]



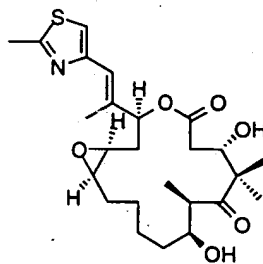
13

(11.53)
[5.63]



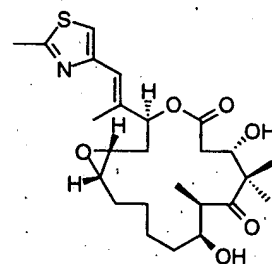
14

(5.42)
[5.75]



15

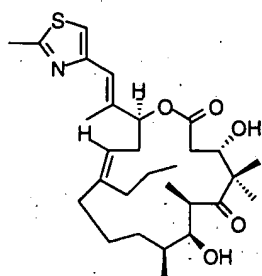
(0.96)
[5.95]



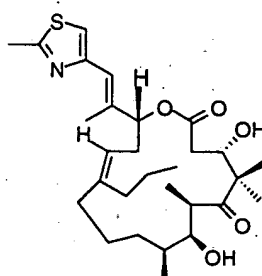
16

(7.47)
[16.48]

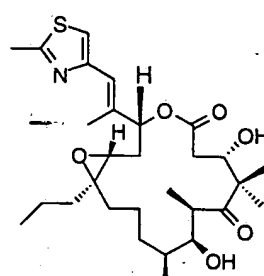
Fig. 40



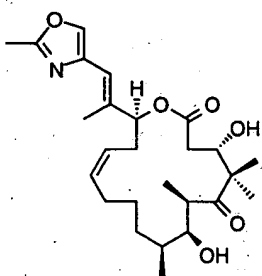
17
(0.090)
[0.254]



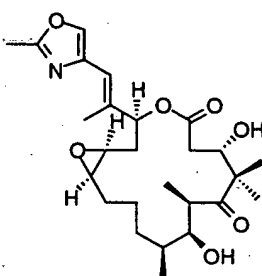
18
(1158)
[>720]



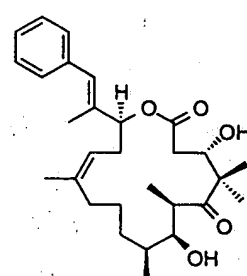
19
(0.96)
[>1.0]



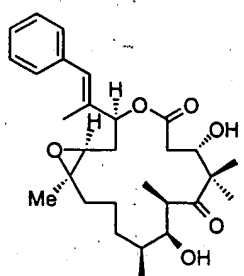
20
(0.030)
[0.049]



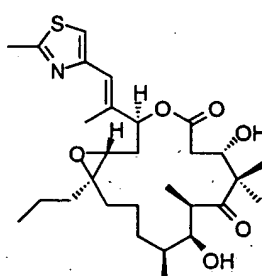
21



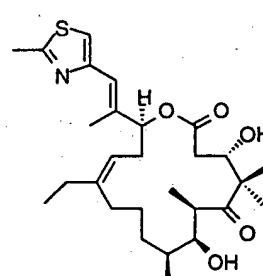
22
(0.098)
[0.146]



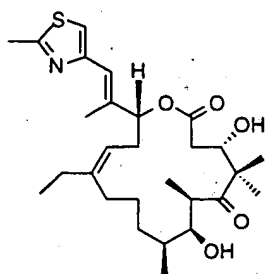
23



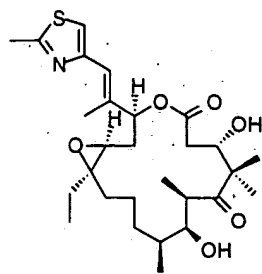
24
(0.0043)
[0.032]



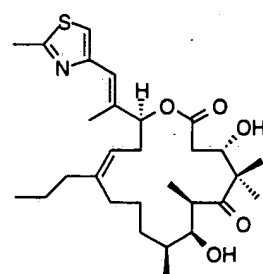
25
(0.021)
[0.077]



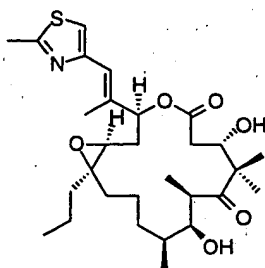
26
(0.055)
[0.197]



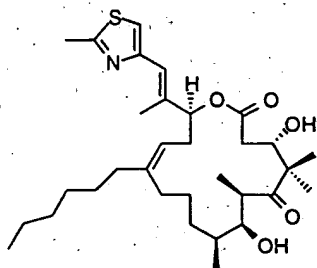
27
(0.0010)
[0.0072]



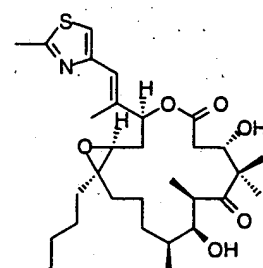
28
(0.039)
[0.067]



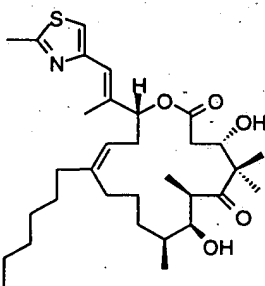
29
(0.0038)
[0.0064]



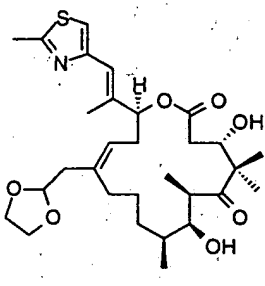
30
(0.044)
[0.108]



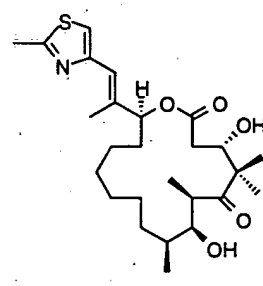
31
(0.027)
[0.049]



32
(0.063)
[0.380]

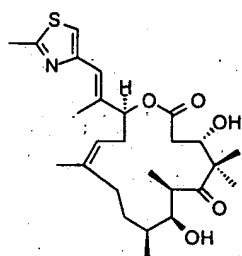


33
(0.0031)
[0.0093]

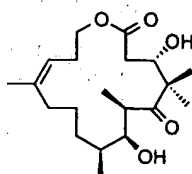


34
(0.143)
[0.276]

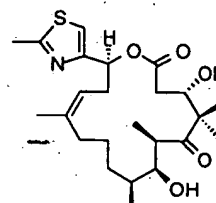
Fig. 42(A)



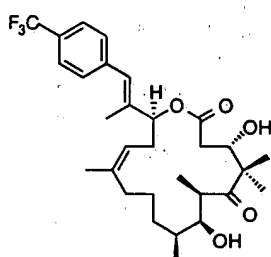
35
(>10)
[8.95]



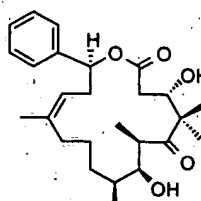
36
(234.5)
[>10]



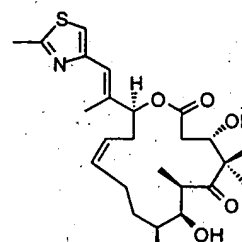
37
(3.25)
[1.20]



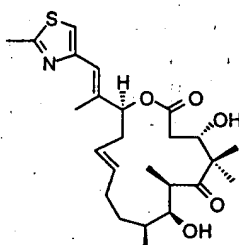
38
(0.254)
[>5.0]



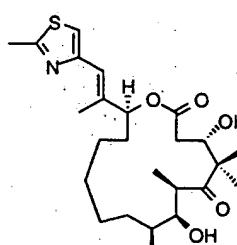
39
(1.80)
[>5.0]



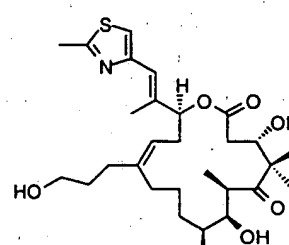
40
(36.9)
[47.3]



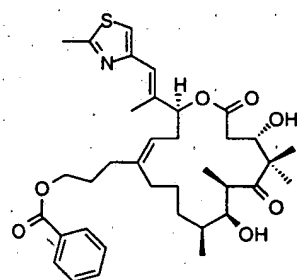
41
(60.1)
[59.2]



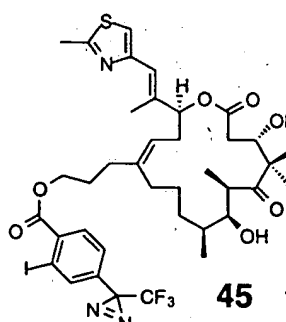
42
(7.41)
[12.9]



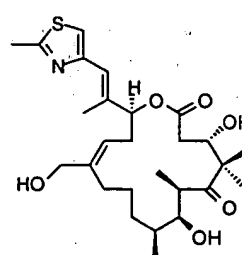
43
(0.0095)
[0.167]



44 (0.250)
[0.905]

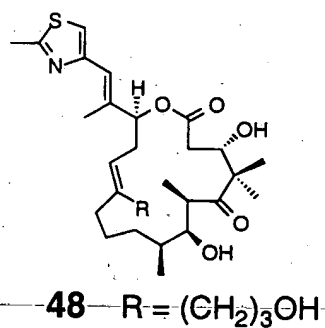
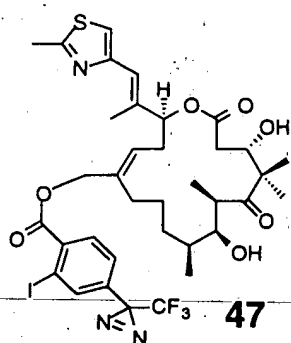


45

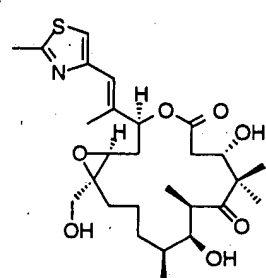


46 (0.049)
[>1.0]

Fig. 42(B)



48 R = (CH₂)₃OH



49

Fig. 42(C)

Fig. 43(A)

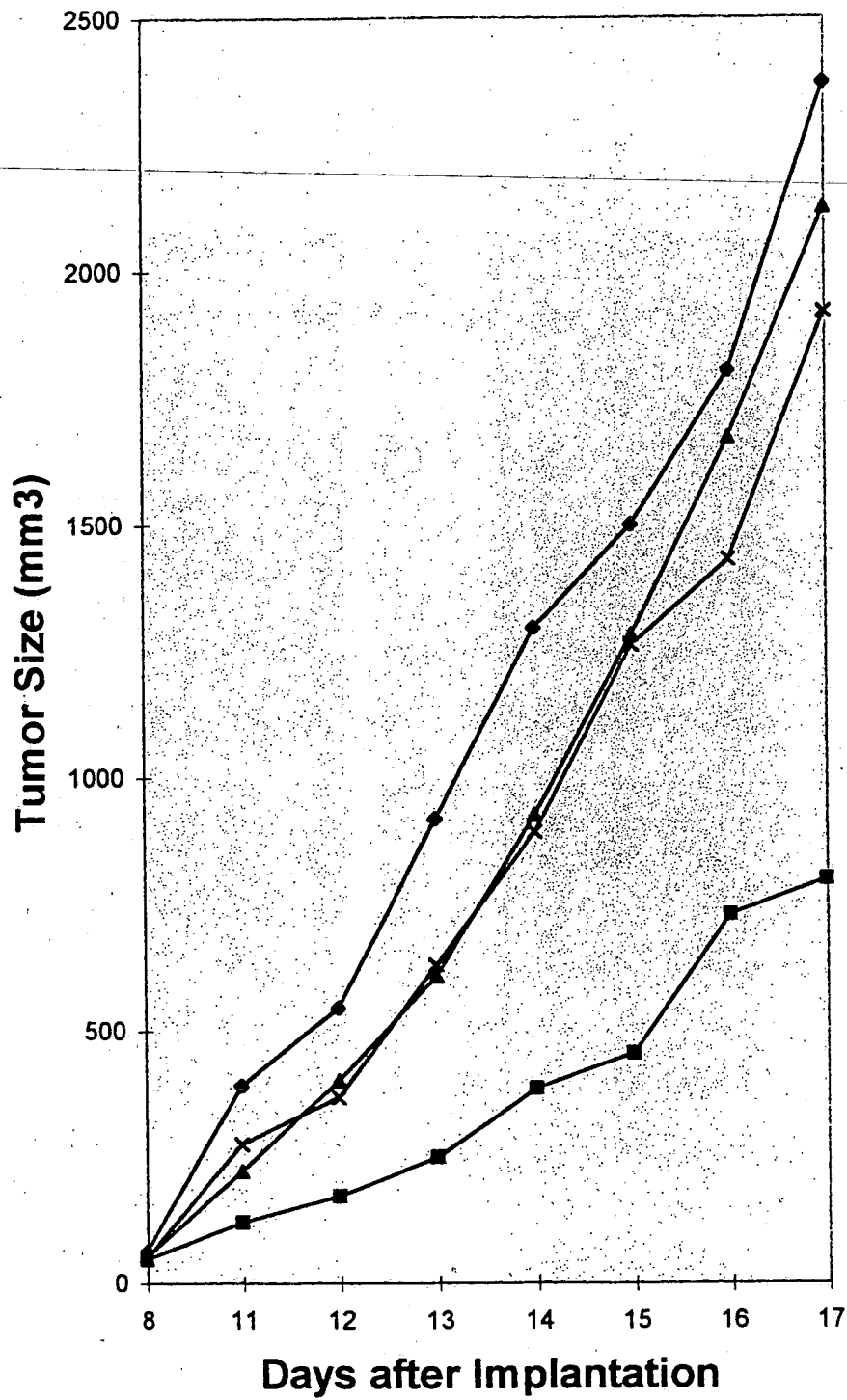
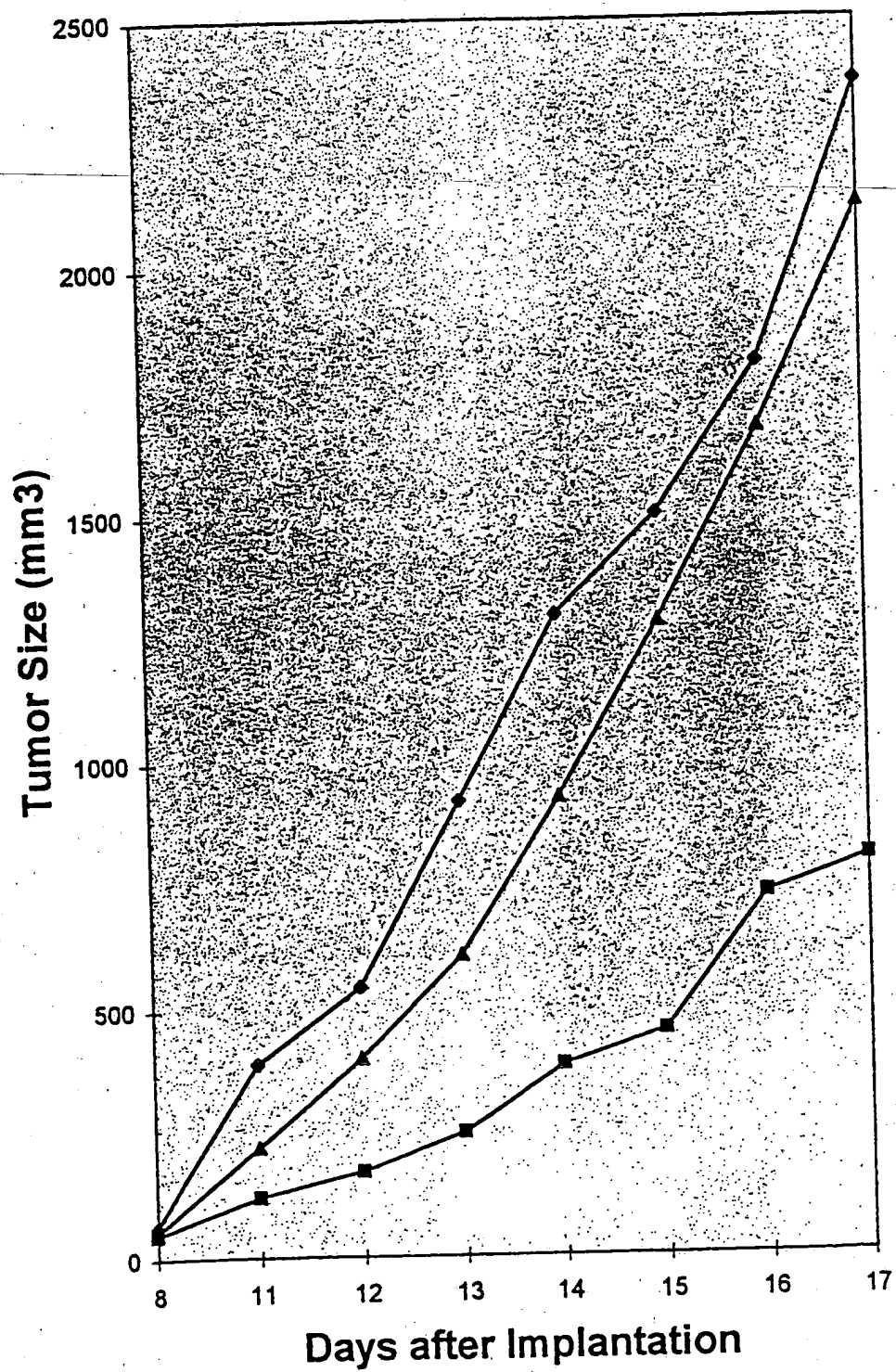


Fig. 43(B)



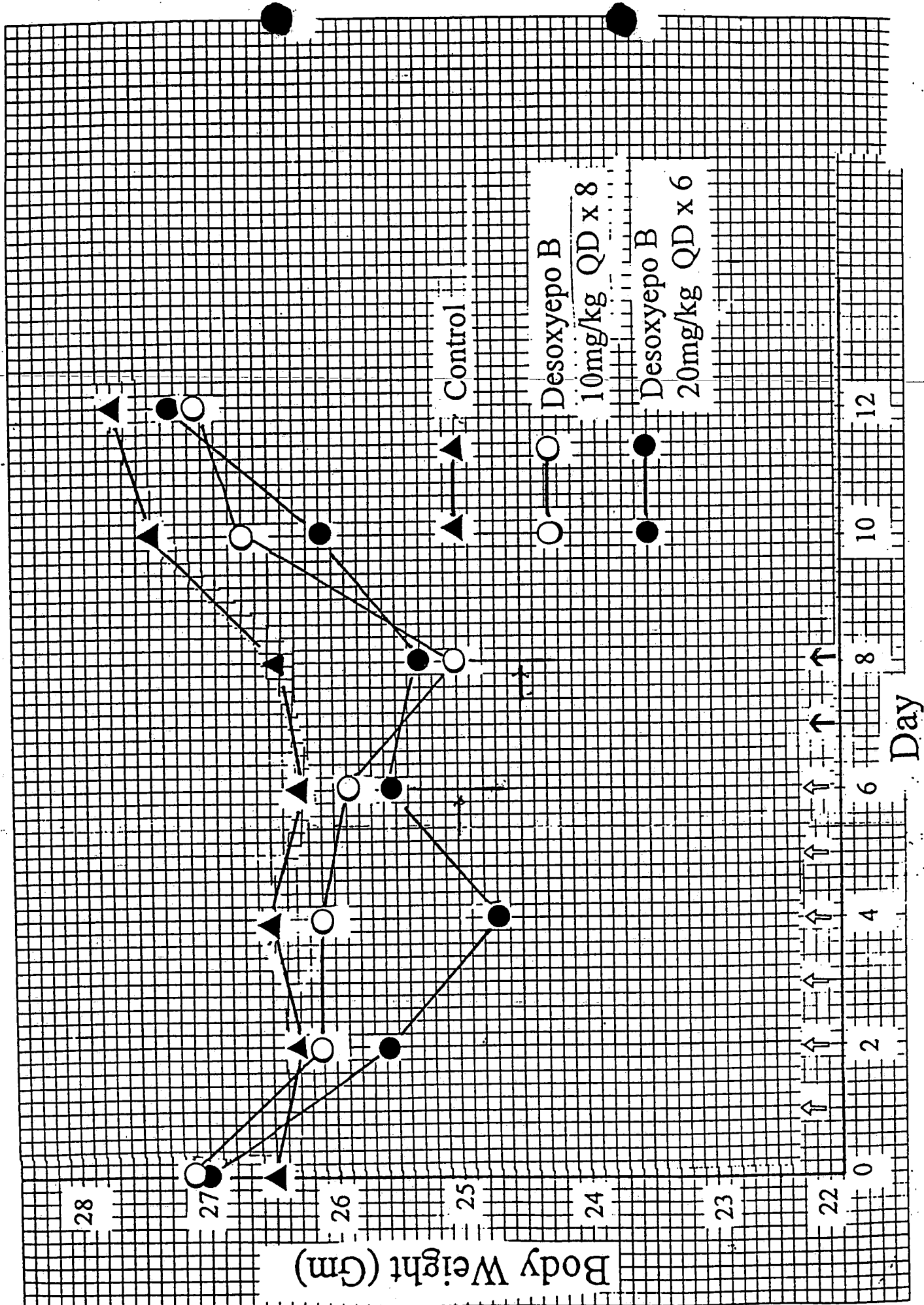


Fig. 44(A)

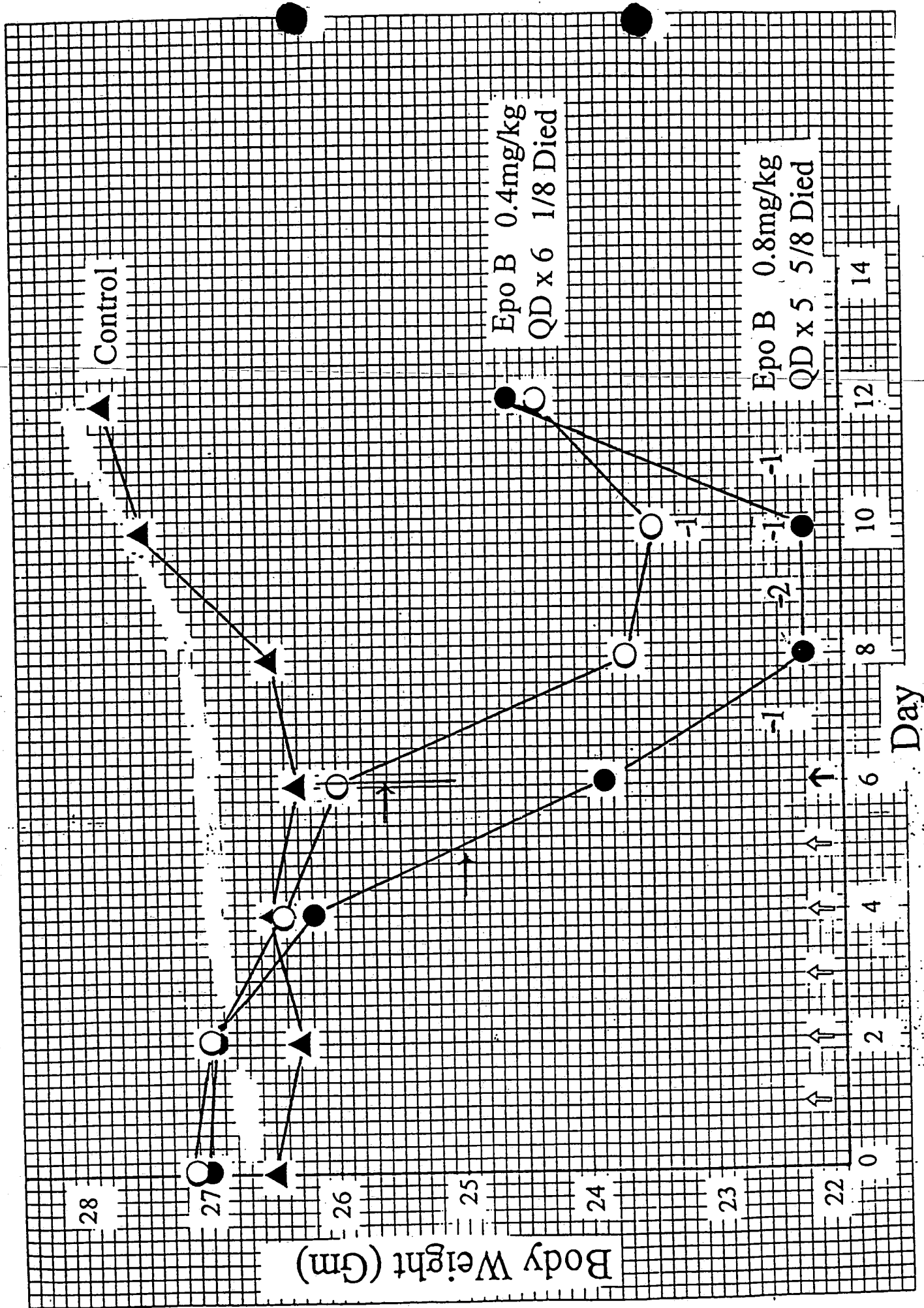


Fig. 44(B)

Fig. 45(A)

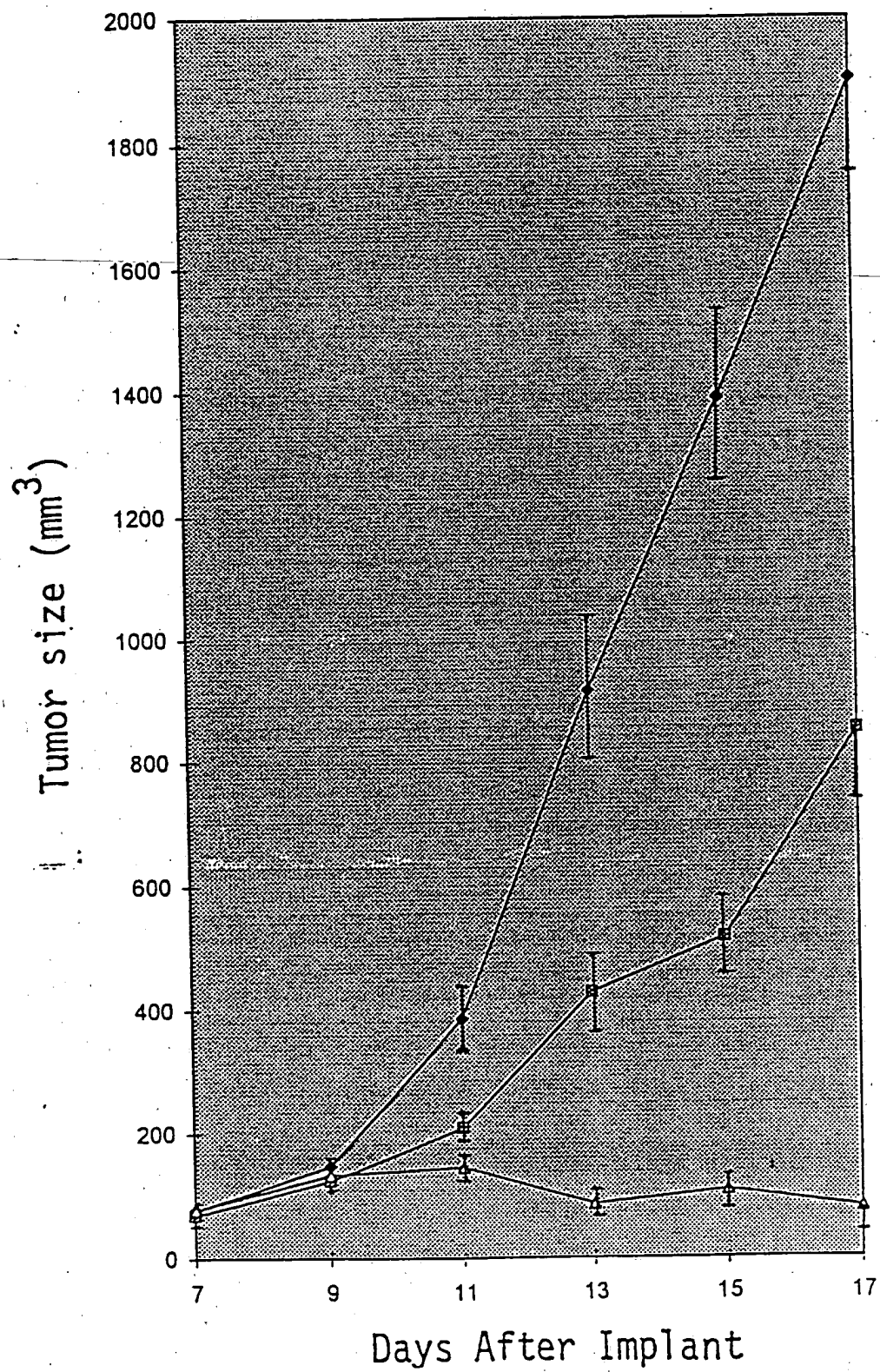
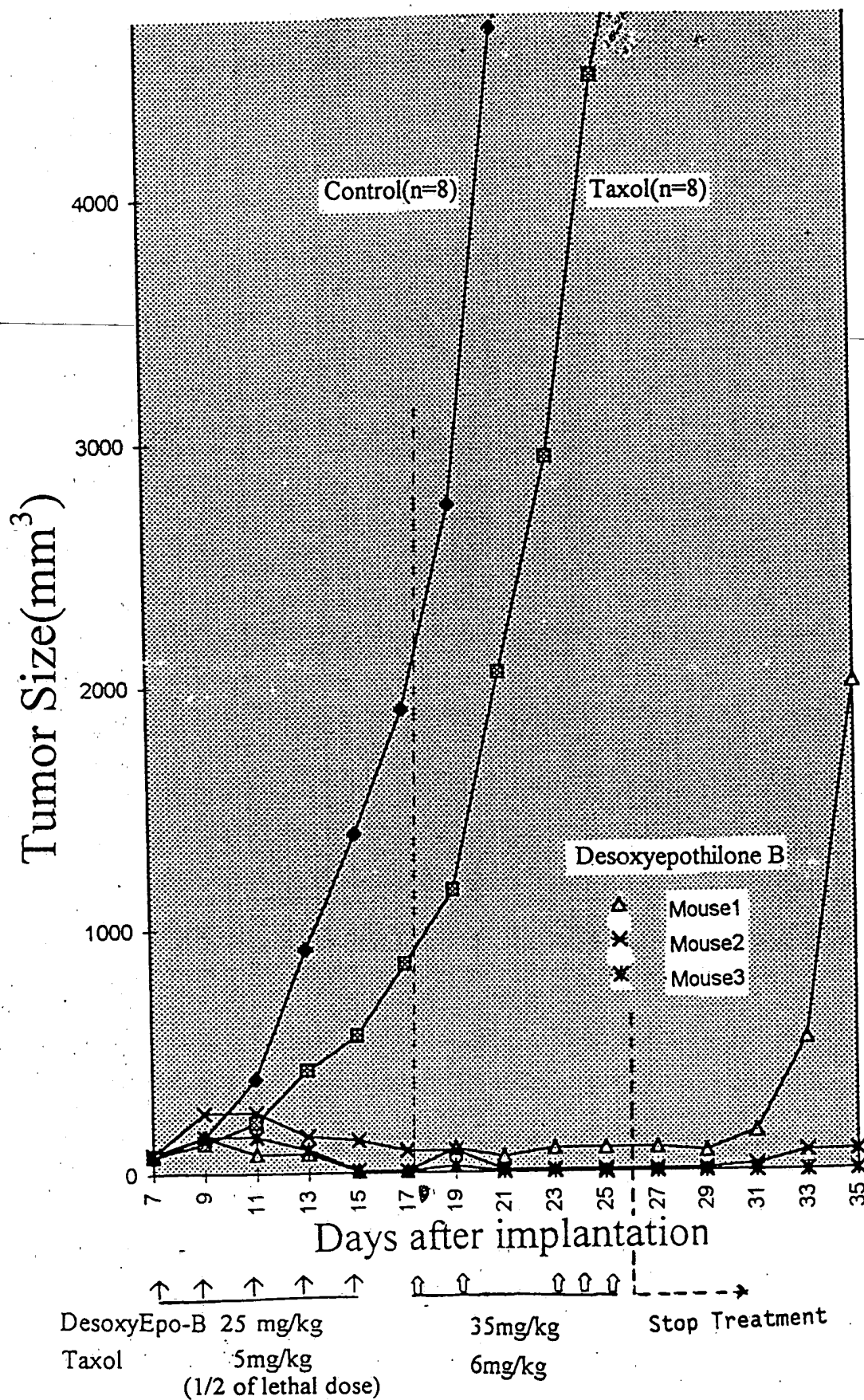


Fig. 45(B)



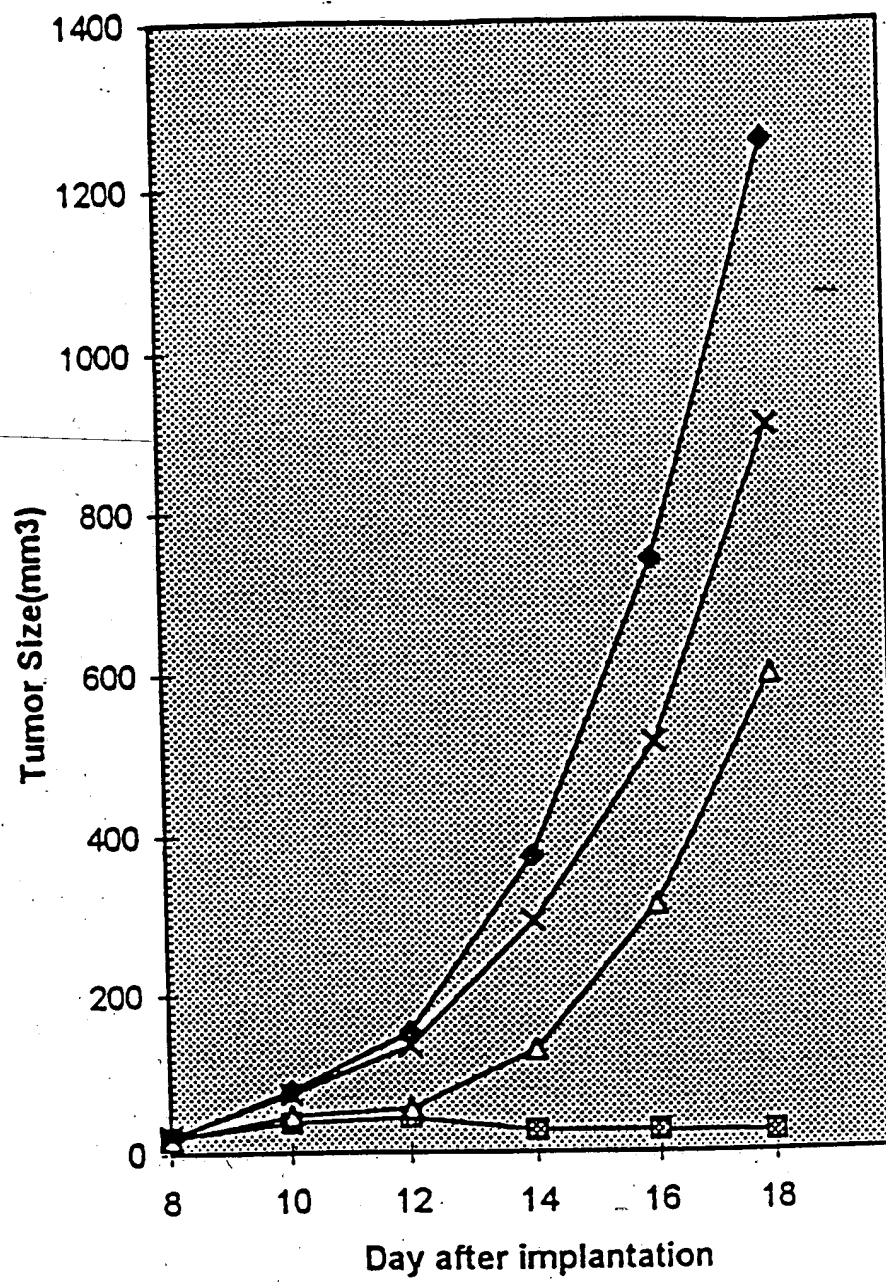


Fig. 46

Fig. 47

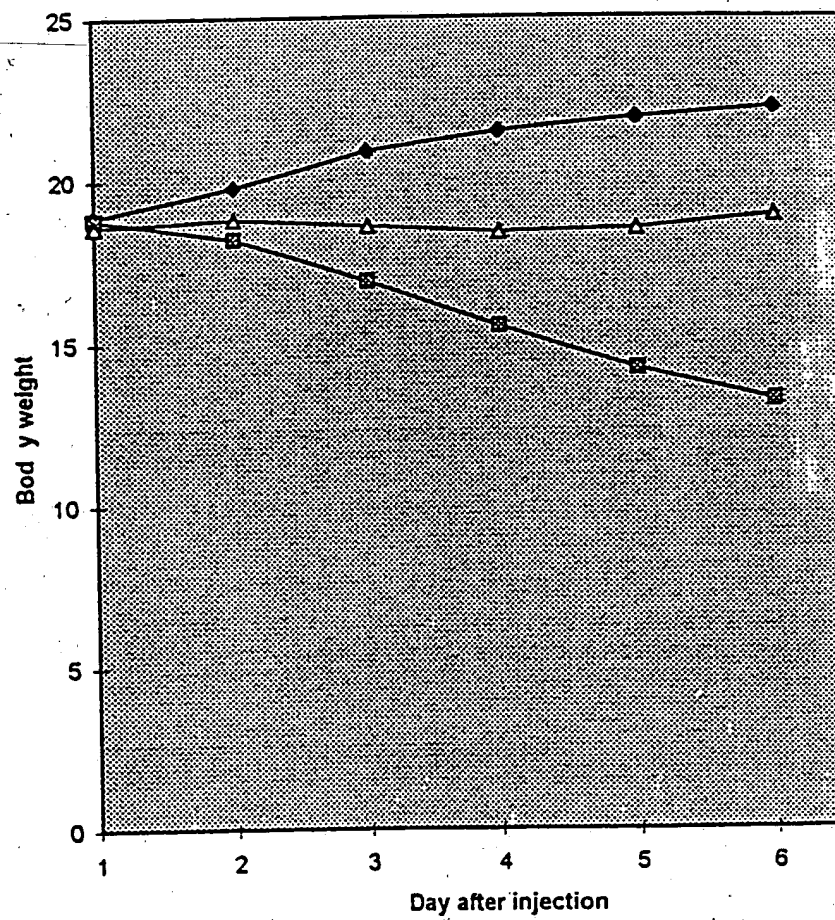




Fig. 48



400 MHz, CDCl_3 , rt.

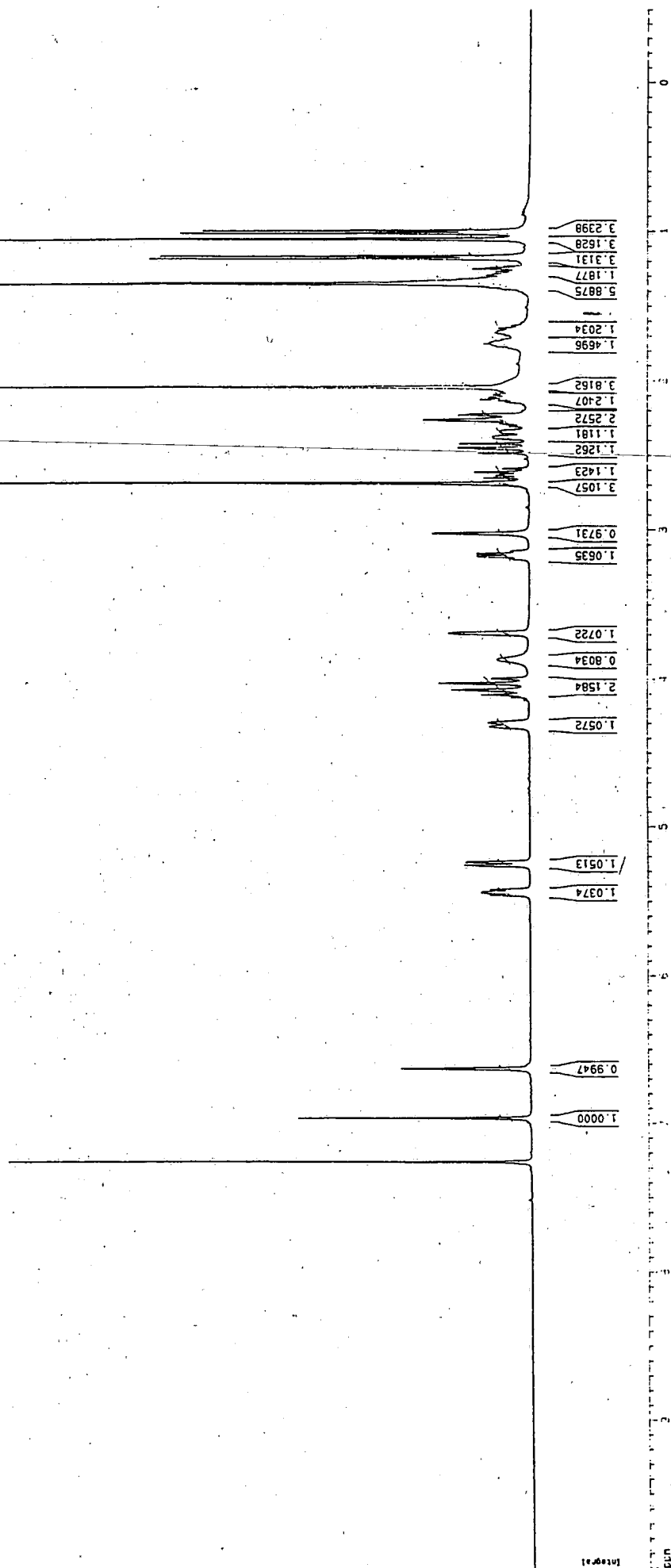
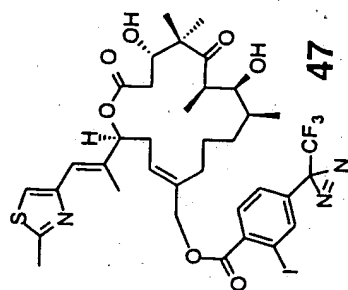


Fig. 50



500 mhz, CDCl₃, rt, crude alcohol mosher

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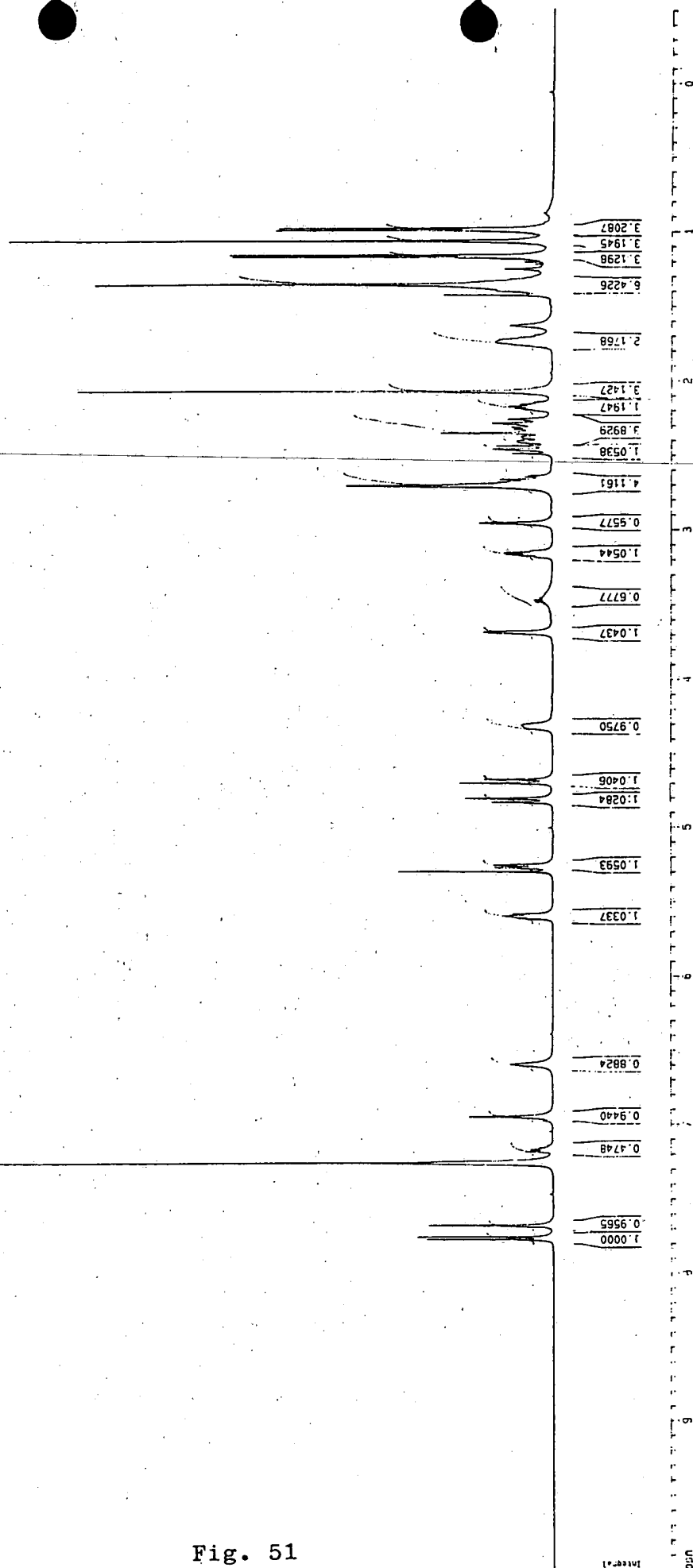
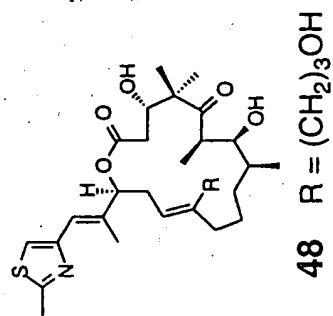


Fig. 51



972.62
938.34
844.53
830.96
815.94
804.86
797.46
783.97
769.34
670.04
650.21
645.50
550.52
528.48
522.42
489.76
482.65
475.49
453.25
447.16
440.36
405.50
396.09
388.61
375.59
368.64
331.37
281.09
15.89
6.14
0.14

2157.59
2156.69
2156.02
2150.63
2131.15
2126.03
2099.94
2055.97
2042.92
2036.33
2029.68
2010.14
1720.22
1710.37
1638.42
1631.26
1624.11

2781.40
2775.14
2740.94
2630.65
2612.46

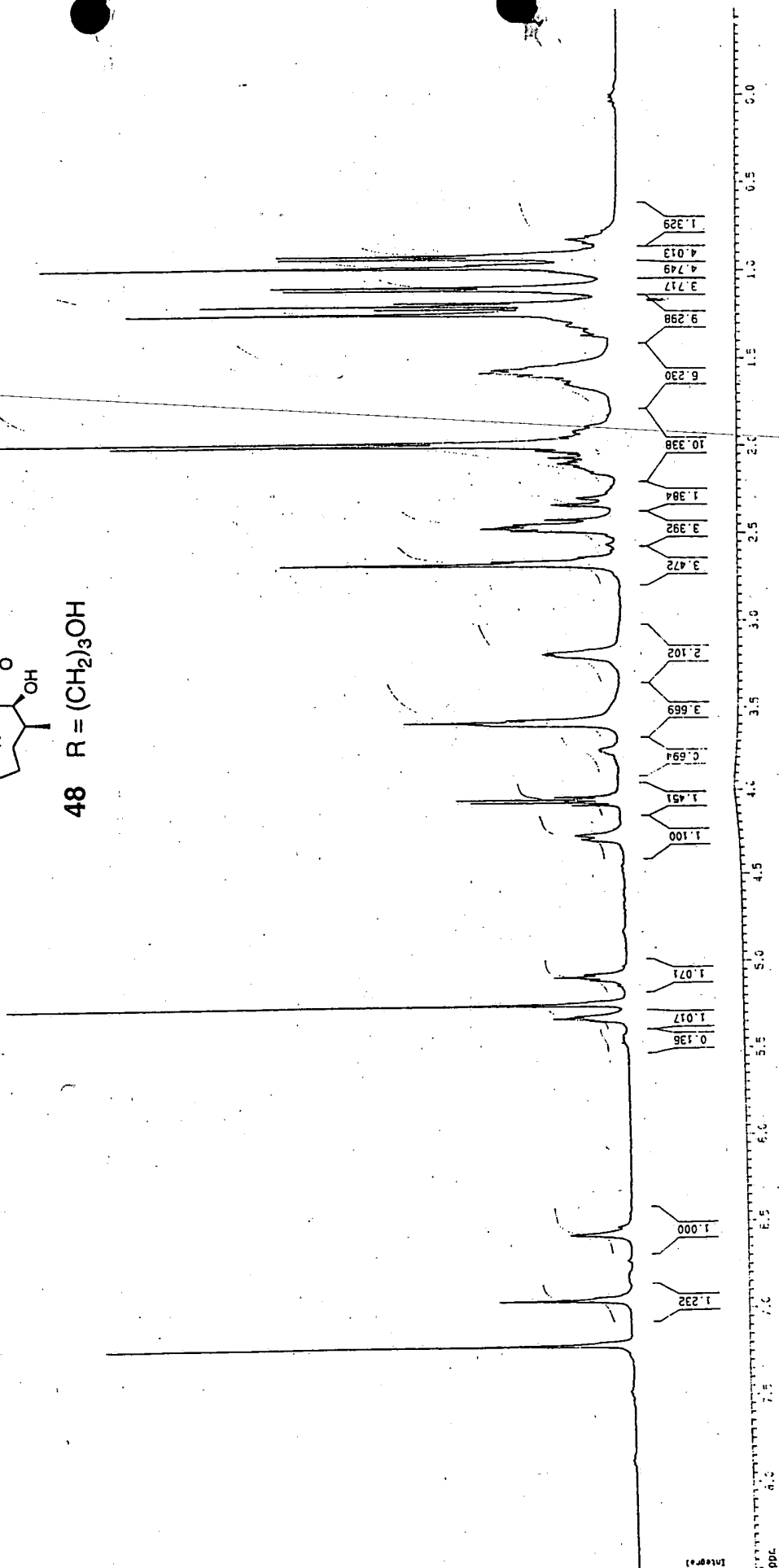


Fig. 52